THE
BRITISH JOURNAL OF SURGERY

VOL. XLIV NOVEMBER, 1956 No. 185

TRANSPLANTATION OF URETERS: AN EXPERIMENTAL STUDY IN DOGS

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DISSATISFACTION with the results of the classical techniques of transplanting ureters to the colon was reflected in genito-urinary circles in recent years by renewed interest in the subject from an experimental point of view. Coffey (1928) quoted F. H. Martin as saying "I am convinced that work on animals will never solve the problems of ureteral anastomosis". Be that as it may, a technique which is manifestly of no value in the dog is hardly likely to be of value in the human subject. The most that experimentalists can hope to do is seek certain principles which, with some modification, can be applied to man. Since we do not believe that the last word has been said on uretero-intestinal anastomosis, and since animal work is bound to be continued at many centres, we thought it advisable to satisfy ourselves that the dog was a reliable animal for studying this problem.

One would have thought that uretero-intestinal anastomosis in the dog would be a straightforward procedure, but a perusal of the American literature dispels this idea. Nesbit (1949) stated "... during the past twenty years we have performed a variety of uretero-intestinal anastomoses upon dogs and the present group of animals are the only ones that have ever survived more than a few days following operation". Schinagel (1948) states "... it is a common experience that it is more difficult to obtain good functional results in the laboratory, with dogs, than in the clinic". Other published data show that difficulties have been encountered at other centres: Hinman (1936), Davalos (1947), Douglass and Edwards (1936), Hinman and Hinman (1950), Weyrauch and Young (1952), and Woodruff, Cooper, and Leadbetter (1952).

Jacobs and Stirling (1952) were impressed by the fact that the post-operative complications in human subjects were related to the pre-operative condition of the patient rather than to the type of anastomosis carried out. This being so, the value of animal experiments is that they can eliminate many of the human variables which have and may continue to confuse any analysis of the problems involved in transplanting ureters. We report here some preliminary results of transplanting ureters of dogs by various techniques to colon and to bladder.

MATERIALS AND METHODS

Dogs of both sexes were used. Weights varied from 12–22 kg. In all 42 dogs were operated on; 35 mongrel and the remainder were greyhounds. The anæsthetic used was intramuscular nembutal (½ gr. per kg. body-weight). The antibiotics used were streptomycin (1 mg. per day intramuscularly) and oral terramycin; these were given on the day prior to the operation and continued for three days after operation. The operations were carried out during the months of March to December. The dogs were observed for periods up to eight months; the individual observation periods are given in the appropriate tables (*see Tables I, II*). The suture material used for the anastomoses was 5/0 silk on an atraumatic needle. The dogs were maintained on a normal meat and biscuit diet and always had free access to water.

In a few dogs intravenous pyelography was performed at weekly intervals after operation. However, this proved to be a difficult procedure and was not continued throughout the experiment.

When the dogs were sacrificed, the following procedure was carried out: the kidneys, ureters, and whatever viscus was attached to them were dissected out in one block of tissue and examined. When the ureters were attached to bowel, both ends of a segment of the latter were ligated. The segment of bowel was then distended with a thin colloidal suspension of barium run in from an open container about 2 ft. above the bench (Micropaque—Damancy & Co.). A similar procedure was carried out when the bladder was attached to the ureters. A radiograph was then taken which indicated clearly whether or not there was any evidence of reflux up the ureters. If no reflux had taken place, colloidal barium was injected at the lower end of the ureter in sufficient amount to outline the renal pelvis and the lumina of the ureters. The barium solution was then removed and replaced by 10 per cent formol-saline. Finally, 10 per cent formol-saline was injected into the lumina of the ureters and the attached viscus; the latter was maintained in a distended state. The specimens were kept in 10 per cent formol-saline for a few days. The specimens were then cut and the intracolonic and intravesical aspects of the

anastomoses were closely examined. Histological sections were made of the kidneys, the ureters, and the anastomoses.

In six instances, the ureters were divided at the usual site for the colonic anastomoses. Immediately after division, a segment of 1 mm. or so was removed from the lower end of the proximal segment of a ureter; 10–15 minutes later a segment was removed from the lower end of the proximal segment. Both segments were immediately fixed in a modified Helly solution for about 2 hours. These specimens were then sectioned for histological examination.

The general plan of the experiment was to evaluate the following techniques:—

1. *Uretero-vesical Anastomosis.*—Ureters were sectioned and reimplanted into the bladder by various techniques—double flap, 12; direct implantation, 6; and by a method akin to the technique for uretero-intestinal anastomosis designed by Leadbetter (1951), 6.

2. *Uretero-intestinal Anastomosis.*—Ureters were sectioned and transplanted to the descending colon at various levels by various techniques—Coffey I, 14; Nesbit, 14; Leadbetter, 6; and direct implantation, 6.

3. *Deviation of Unsectioned Ureters through a Coffey Tunnel in the Descending Colon.*—This really amounted to the first step of the Coffey-Higgins procedure which aimed at later implanting the ureter in the bowel.

4. *Autotransplantation of a Kidney to the Iliac Vessels.*—Unilateral nephrectomy was performed. The other kidney was removed and autotransplanted to the iliac vessels by a technique described elsewhere (Dempster, 1954; Dempster, Joekes, and Oeconomos, 1955). The ureter was sectioned where it crosses the iliac vessels and was reimplanted into the bladder by the double-flap technique; in one instance the direct implantation technique was used. Seven autotransplantations of kidneys were done in greyhounds.

TECHNIQUES OF ANASTOMOSIS

1. Uretero-vesical Anastomosis.—Except for those experiments involving autotransplantation of kidneys, the ureter was divided close to the bladder and mobilized for about 4 cm. The anastomosis was made in all instances into the superior aspect of the posterior surface of the bladder. When the double-flap method was used, the lower end of the ureter was split on each side for about 3 mm. and each flap was fixed to the bladder by a through-and-through suture. When the direct technique was used, the end of the ureter was transfixed by a stay suture which held the ureter in place within the bladder while the anastomosis was performed. The stay suture was later removed. The aim was to project about 0·5 cm. of ureter within the bladder. Fixation of the ureter to the mucosa of the bladder was carried out as follows: the bladder mucosa, which was always redundant, was drawn up, tent-wise, above the level of the serosa and stitched to the adventitia of the ureter. In this way the ingoing ureter was clothed for about 0·5 cm. with mucosa and adventitia of the bladder, constituting, in fact, a short tunnel for the ureter. Care was always taken to stitch the ureter loosely to the bladder because a ureter swells after being sectioned. When the Leadbetter technique was used a tunnel of partial thickness of the bladder wall was used. When the Nesbit technique was used, the peritoneal covering of the bladder was loosely stitched over the anastomosis.

2. Uretero-intestinal Anastomosis.—

a. Coffey I: Fat surrounding the lower end of the sectioned ureter was always carefully removed. The bowel mucosa was brought up, tent-wise, and stitched to the adventitia of the ureter with the object of preventing retraction of the ureter. There was always an interval of at least 20 minutes between sectioning the ureters and their being laid in the submucous tunnel.

b. Leadbetter: No modifications of the original procedure were employed.

c. Direct implantation: The end of the sectioned ureter was drawn into the lumen of the bowel by a stay suture which was later removed. The aim was to project about 1 cm. of ureter within the bowel. The mucosa of the bowel was drawn up tent-wise and loosely stitched to the adventitia of the ureter. The serosa of the bowel was loosely stitched round the ureter since some œdema develops within the tunnel due to trauma.

d. Nesbit: The anastomosis was performed as originally described (1949).

In all these experiments, the peritoneum on each side of the ureter was divided parallel to it. A narrow strip of peritoneum was left covering the front and sides of the mobilized ureter.

3. Laying the Undivided Ureter in a Coffey Tunnel.—The ureter on one side was mobilized for about 4 cm. at the level of the pelvic brim. An oblique incision was made into the submucosa of the colon and a tunnel about 3 cm. long was prepared into which the mobilized segment or ureter was laid. The bowel serosa was loosely stitched over the ureter. The contralateral ureter acted as the control.

RESULTS

The Effect of sectioning a Ureter.—Immediately a ureter is sectioned a swelling occurs at the distal end of the proximal segment. This swelling continues and reaches a peak about 15 minutes afterwards (*Fig.* 277 C, D). The swelling is mainly caused by an œdema of the advential coat of the ureter. In addition, ureteric peristalsis becomes more frequent and vigorous. No interference with the ejection of urine ensues. This can easily be confirmed by observing the ureter for about 5 minutes and noting the urine stain on the swab enclosing it. A similar phenomenon occurs in the human ureter after being sectioned (*Fig.* 277 A, B), but the rate at which the maximum swelling occurred has not been determined.

The Effect of the Anastomosis on the Physical State of the Kidneys and Ureters.—The results will be classified as good or bad according to whether little or no change or obvious hydroureter or hydronephrosis had developed.

Group 1. Uretero-vesical Anastomosis.—

a. Double-flap technique: 11 anastomoses were performed; all results were good.

b. Direct implantation: 6 anastomoses were performed; 1 bad result and the remainder were good.

c. Leadbetter technique: 6 anastomoses were performed; all were bad.

d. Nesbit technique: 6 anastomoses were performed; all results were good.

Group 2. *Uretero-intestinal Anastomosis.*—

a. Coffey I technique: 14 anastomoses were performed; there were 8 good, 5 moderately good, and 1 bad result.

b. Direct implantation: 6 anastomoses were performed; 4 good and 2 bad results were obtained.

c. Nesbit technique: 12 anastomoses were performed; all were good.

3. The effect of deviating the ureters through a Coffey tunnel would appear to be slight. The same procedure in the human, it will be recalled, was also uneventful.

The problem is, however, somewhat more complicated and there are other factors to be considered. The following factors will be analysed with a view to determining which of them influenced the development of hydronephrosis and hydro-ureter.

1. Local Infection at the Site of the Anastomosis.—In only 2 instances was there any evidence of local extension of infection from the actual anastomotic site. The extension of local infection was a feature stressed by Hinman and Weyrauch (1942). One occurred in Group 1 (*a*) (double-flap technique) and the other in Group 2 (*b*) (direct-implantation technique); in neither instance was there more than mild hydronephrosis. The usual limit of local infection was confined to the junction of ureter and colon. The ureter in the Coffey tunnel was clear of any signs of infection. There were only 4 instances of acute pyelonephritis, whereas in most instances there were local signs of infection at the junction of ureter and colon. This suggests that the local infection at the anastomosis does not usually ascend the ureter.

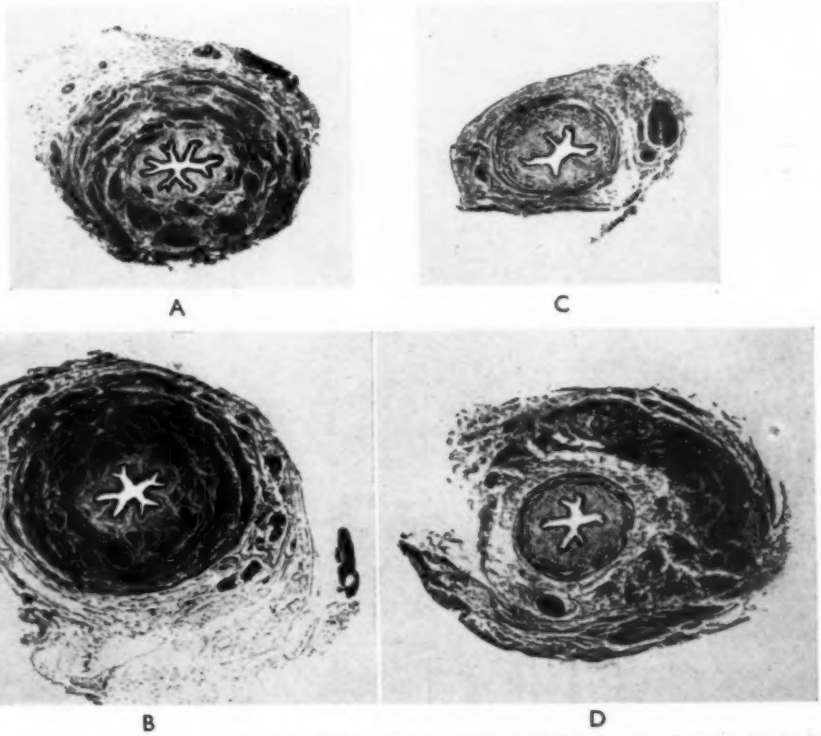

FIG. 277.—A, B, Photomicrograph of a human ureter immediately after section and again after 15 minutes. C, D, Photomicrograph of dog ureter immediately after section and again after 15 minutes. H. & E. (× 9·5.)

d. Leadbetter technique: 6 anastomoses were performed; all were good.

Group 3. *The Effect of the Deviation through a Coffey Tunnel.*—All four ureters which were so deviated showed mild dilatation compared with the contralateral ureters. Any obstruction which may have developed in the Coffey tunnel did not lead to any signs of acute pyelonephritis. The contralateral kidneys provided histological control.

CONCLUSIONS

1. Uretero-vesical anastomoses: Since the Leadbetter and direct implantation techniques can lead to bad results they are not advisable for use in dogs. Since the double flap gave good results and is simple to perform, it is the method of choice in dogs.

2. Uretero-intestinal anastomoses: The Leadbetter and Nesbit methods gave uniformly good anatomical results, but poor clinical results followed the Nesbit operation. Direct implantation and Coffey I techniques can lead to bad results and hence the Leadbetter technique is the one of choice in dogs.

2. The Effect of the Healing Process in the Coffey Tunnel.—The results of the experiments in Group 3 indicate that the healing process, *per se*, has little if any adverse effect on the ureter and kidney. There was no histological evidence of more than minimal fibrosis within the tunnel in either this group or in Group 2. Furthermore, it is evident that fibrous tissue contraction or angulation and kinking of the ureter on emerging from the tunnel

has no consistent effect on the development of hydro-ureter or hydronephrosis.

3. Site of Anastomosis to the Colon.—In Group 2 (*a*), that is in the Coffey I series of anastomoses, opportunity was taken to vary the site of union of the ureter with the colon. It is essential in this type of experiment to section the ureters at a definite site in all instances; the site chosen was the brim of the pelvis. The colon of the dog is very mobile and so one can easily pull the colon up or down as required. From the results of the small series of experiments, it could be interpreted that the lower in the colon the ureter was implanted, the more constant and the more severe the resulting hydro-ureter and hydronephrosis. There was slight evidence that ureters placed high in the colon showed no hydronephrosis or hydro-ureter even though the kidneys showed signs of chronic canine nephritis (*Table I*).

When hydronephrosis developed, it did so rapidly. It is easy to demonstrate this by pyelography at weekly intervals after operation; such a procedure is seldom feasible in the human. A hydronephrosis after ureteric transplantation may remain stationary, regress, or progress. We must confess that ureteric transplantation can provide one with an excellent technique for the study of hydronephrosis!

4. Chronic Canine Nephritis.—It is important to be acquainted with this condition. It is a reality

Table I.—THE RELATIONSHIP BETWEEN PRE-EXISTING CANINE NEPHRITIS AND THE DEVELOPMENT OF HYDRONEPHROSIS AND HYDRO-URETER FOLLOWING URETERAL ANASTOMOSIS

Series	Dog Number	Days Observed	Pre-existing Chronic Canine Nephritis		Hydro-ureter after Anastomosis		Hydronephrosis after Anastomosis	
			Right	Left	Right	Left	Right	Left
Group 1			*Uretero-vesical Anastomosis*					
a. Double-flap method	1	30	+	C	+	C	–	C
	2	30	C	–	C	+	C	–
	3	70	+ APN	C	+	C	+	C
	4	30	C	+	C	+	C	–
b. Direct implantation	1	30	C	–	C	+	C	–
	2	30	–	C	–	C	–	C
	3	70	C	+ APN	C	–	C	–
	4	30	C	+	C	+	C	–
	5	30	C	–	C	+	C	+
c. Leadbetter	1	30	+ APN	+	+	+	+	+
	2	30	+	+	+	+	+	+
	3	60	+	+	+	+	+	+
Group 2			*Uretero-intestinal Anastomosis*					
a. Coffey I	1	30	+	+	+	–	+	+
	2	50	+	+	–	–	+	+
	3	30	+	+	+	+	+	+
	H 4	40	–	–	–	–	–	–
	5	30	+	+	+	+	+	–
	6	40	+ APN	+ APN	+	+	+	+
	7	40	+	+	+	+	+	+
b. Direct implantation	1	30	+	+	+	+	+	+
	2	50	+	+	+	+	+	+
	3	30	+	+	+	+	+	+
c. Nesbit	1	14*	–	–	–	–	–	–
	2	13*	–	–	–	–	–	–
	3	30	–	–	–	–	–	–
	4	7*	–	–	–	–	–	–
	5	21	+	+	–	–	–	–
	6	4*	–	–	–	–	–	–
d. Leadbetter	1	40	+	+	+	+	+	+
	2	30	–	–	–	–	–	–
	3	30	+	+	–	–	+	–
Group 3								
Deviation of a ureter through a Coffey tunnel	1	30	C +	+	–	+	–	+
	2	30	C +	+	–	–	–	+
	3	30	C –	–	–	+	–	–
	4	70	C +	+	–	+	–	+

APN = Acute pyelonephritis.
* = Died
C = Control
H = The ureters were anastomosed to a position high up on the colon.

Total number of mongrel dogs 35

a. Number of dogs free from canine nephritis 12
Number of dogs showing dilatation of ureter and renal pelvis after ureteric transplantation 3

b. Number of dogs with canine nephritis 23
Number of dogs with canine nephritis showing dilatation of ureter and renal pelvis after ureteric transplantation 20

(Broom and McIntyre, 1948 ; Platt, 1951 ; McIntyre and Montgomery, 1952 ; Dempster, 1953). In its chronic form, the basement membrane of the glomeruli shows thickening and there are usually subcapsular scars and this may or may not be associated with a plasma-cell infiltration (*Fig.* 278). Acute pyelonephritis, such as could occur in the first few weeks after uretero-intestinal anastomosis, is a polymorphonuclear leucocyte infiltration affecting the pelvis as a direct downward spread from the

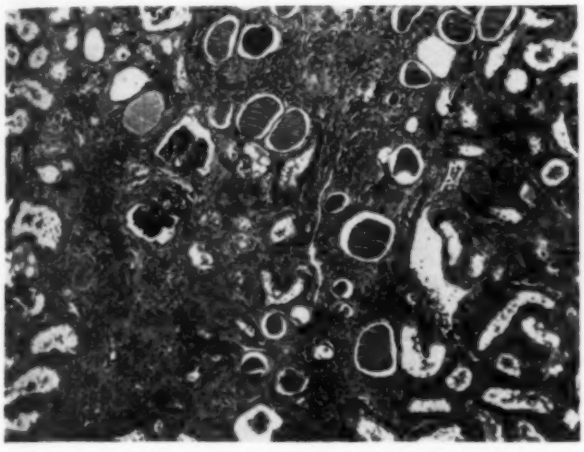

FIG. 278.—Photomicrograph of a dog kidney showing typical signs of chronic canine nephritis—fibrous tissue reaction, plasma cells, thickening of glomerular basement membrane, and dilated tubules. H. & E. (× 57·5.)

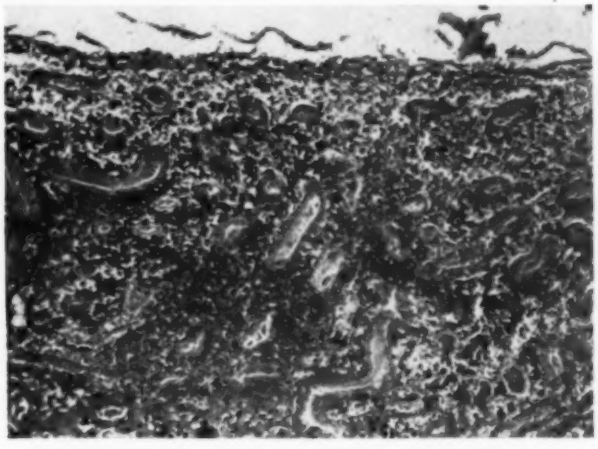

FIG. 279.—Photomicrograph of a dog kidney showing acute pyelonephritis following anastomosis of its ureter to the colon. An area through the outer cortex and capsule is shown heavily infiltrated with polymorphs. H. & E. (× 95.)

cortex (*Fig.* 279). This acute pyelonephritis is easily distinguished from acute or chronic canine nephritis. Out of 23 instances where unmistakable signs of pre-existing chronic nephritis existed in the kidneys, hydro-ureter and hydronephrosis developed in varying degree in 20 (*Table I*). This applies to all techniques but refers only to the 35 mongrel dogs used in these experiments ; only greyhound kidneys were used in the transplanted kidney series because of the low incidence of canine nephritis in this breed. Out of the remaining 12 mongrels which showed no signs of past canine nephritis, only 3 developed mild to moderate degrees of dilated ureter and renal pelvis (*Table I*). Out of 35 mongrel dogs operated on, evidence of acute pyelonephritis following the transplantation of ureters was found in 5 kidneys (4 dogs).

5. Reflux up the Ureter.—In Group 1 (*a*) (double-flap technique) reflux occurred once. Reflux occurred consistently in Group 2 (*c*) (Nesbit technique) ; in no instance, however, did hydro-ureter or hydronephrosis develop. The fact that no reflux was observed in 2 instances in the Nesbit series may indicate that if the stoma is small enough, this complication need not occur.

Reflux in this context refers to the passage of colloidal barium from a distended segment of gut at autopsy. The distension employed may have grossly exaggerated the normal range of distension naturally occurring in the intact animal. The fact that reflux occurred under those conditions only in the Nesbit series was of value experimentally. All kidneys in this particular group were free from canine nephritis. There were no signs of pyelitis and this would suggest

Table II.—SERUM CHEMISTRY (PRE- AND POST-OPERATIVE) OF DOGS IN THE COFFEY† AND NESBIT GROUPS

DOG NUMBER	GROSS STATE OF KIDNEYS		BLOOD-UREA mg. per cent		SERUM CHLORIDE m.Eq./L.		SERUM SODIUM m.Eq./L.		SERUM POTASSIUM m.Eq./L.		Co^2 CP m.Eq./L.	
	Pre-op.	Post-op.	Pre-op.	Post-op.	Pre-op.	Post-op.	Pre-op.	Post-op.	Pre-op.	Post-op.	Pre-op.	Post-op.
Coffey operation												
1	Good	Poor	25	88·5	130	134	175	174·6	3·8	4·3	22	24·8
2	Good	Fair	30	178·3	120	121·5	170	179	3·5	4·6	24	29·7
3	Good	Poor	28	44	119	116	171	152	4·15	3·14	25·2	24
4	Good	Good	11	156	130	128	170	151	3·8	3·3	24	16
5	Good	Poor	25	218	132·5	122	170	158	3	3·5	22	24
6	Good	Poor	31	160	123·5	127	161	160	4·1	4	22	22
7	Good	Poor	32	627	123	120	171	164	3·9	3·5	25	25
Nesbit operation												
1	Good	Good*	21	—	121	—	174	—	4·4	—	25	—
2	Good	Good*	32	—	117	—	167	—	3·5	—	24·8	—
3	Good	Good	23	41	128	119	181·8	155	4·2	4·12	24·3	27
5	Good	Good	14	263	128	125	172	158	4·1	6·4	24	22

* Dog died.

† It will be noticed that in spite of severe damage to the kidney soon after the operation in the Coffey series, no instances of hyperchloræmic acidosis developed. This can be explained in part by the fact that the dog kidney is better able to excrete sodium chloride than is the human kidney.

that reflux does not necessarily lead to pyelitis and pyelonephritis; one does not necessarily have to conclude that pyelitis resulted from an ascending infection. There is no proof that reflux of fæcal contaminated urine or air did occur in the intact animal in these experiments. It is seldom possible to observe gas in the renal pelvis in the dog because of the difficulty of preparing the dogs for such studies.

CONCLUSIONS

There appears to be a relation between the site of anastomosis and the original histology of the kidney and the subsequent development of hydronephrosis and hydro-ureter. There was some slight evidence to confirm the suggestion of Baker and Miller (1952) that ureters placed high in the colon give better results than those placed low down. Pre-existing chronic nephritis does not necessarily predispose to the development of acute pyelonephritis following transplantation of ureters.

Serum Chemistry.—This aspect was not followed in detail in all experiments. Data are available from the Coffey and Nesbit experiments (*Table II*); detailed data on the autotransplanted kidneys are given elsewhere (Dempster, Joekes, and Oeconomos, 1955); in these latter experiments the serum chemistry was essentially normal after the third week. The blood-urea rose in the dogs in the Coffey and Nesbit experiments, but the other values were in the normal range for the dog.

Results assessed on the Clinical Condition following Operation.—Except for the dogs in the Nesbit series, all others made an uneventful recovery and appeared not to be upset by the operation. The dogs in the Nesbit series vomited repeatedly, drank water, and refused food, and 2 died about a week after operation. They passed urine per rectum. This indicates that anatomical perfection after operation need not necessarily indicate a smooth clinical course. The difference in behaviour of this group of dogs is rather difficult to interpret. The Nesbit series was carried out in the winter months during a cold spell.

All dogs quickly gained some control of evacuation, which occurred about 3-hourly. The wounds all healed well. No urine leakage, peritonitis, or sloughing of the ureter occurred. The blood-supply of the dog ureter is generous and so one is not faced with the difficulties which are thought might occur in the human (Daniel and Shackman, 1952).

The Effect of Urine on the Bowel Mucosa.—There was no evidence that any gross change occurred in the colonic mucosa. In some cases some local atrophy of the colonic epithelium was noted but this was considered to be non-specific.

Shortening of the Ureter following Section and Anastomosis to Colon or to Bladder.—That the ureter shortens following section and anastomosis was clearly demonstrated in the series of autotransplanted kidneys (Dempster, Joekes, and Oeconomos, 1955). In this series, the ureters were sectioned where they crossed the iliac vessels. The ureter was then re-implanted into the bladder after the kidney had been transferred to the pelvis. After several months, the ureters were seen to have taken up the slack, as it were, and now were of a length sufficient to bridge the short gap between bladder and kidney. This shortening may be significant in the anastomoses to colon since there is some thin evidence that ureters cut at the same site and placed high in the colon may give better results than those placed low in the colon.

DISCUSSION

To what extent is uretero-intestinal and uretero-vesical anastomosis comparable in man and dog? We submit that there is a good deal in common. Urologists have noted many reasons for failure of uretero-intestinal anastomoses. There is some general clinical agreement about the best method of performing ureteric anastomosis to the bladder and this supports our conclusions about the double-flap procedure in the dog. Leakage and peritonitis (Shackman, 1947) used to be formidable complications following uretero-intestinal anastomosis in the human but are no longer of importance; this was our experience in dogs. This fact might settle a certain doubt voiced by Cordonnier (1952): "The problem of urinary leakage, for instance, which seems to present a distinct hazard in the experimental animal has not been present at the site of anastomosis. Therefore I am not wholly convinced that the experimental findings which have been presented would necessarily apply in the human." We did not experience in dogs the difficulties reported by several American experimentalists; another series of experiments by colleagues in this laboratory was similar to our own (Shackman, Daniel, and Lennox, 1952).

Three other reasons for failure may be considered:—

1. Obstruction at the tip of the ureter where it joins or projects beyond the bowel mucosa.
2. Obstruction in the Coffey tunnel caused by scarring and infection.
3. Obstruction caused by angulation or fibrous stricture at the point where the ureter enters the Coffey tunnel.

Our results would reject (2) and (3) as being unimportant; except for certain disasters with the direct-implantation technique, (1) is also relatively unimportant.

It is rather difficult to assign any significance to the swelling of the ureter following section (*Fig. 277*). It is interesting, however, that urologists have not commented upon this phenomenon since it does occur in the human ureter. It may be significant in a context noted by Riches (1949), "The desire to avoid leakage has sometimes led to excessive suturing with consequent compression of the ureter". However, in our discussions with colleagues, we have gained the impression that compression of a swelling ureter in a Coffey tunnel does not explain the post-operative oliguria which is frequently noted. Post-operative oliguria, bilateral or unilateral, may occur in spite of catheters placed in the pelves of the kidneys at the time of operation.

The pre-operative condition of the kidney is perhaps the most important factor in determining success or failure of any technique of anastomosing a ureter to the bowel. The correlation between the incidence of chronic canine nephritis and the subsequent dilatation of the ureter and renal pelvis, may explain the apparently inexplicable results of other authors.

One group of workers was unable to explain the following: "In several instances severe pyelonephritis was found to be present despite adequate flow rates and seemingly adequately function anastomoses" (Woodruff, Cooper, and Leadbetter, 1952). It is quite probable that the severe pyelonephritis was a pre-existent lesion.

Hyperchloræmic acidosis may occur soon or years after uretero-intestinal anastomosis. (*See* note to *Table II.*) If there has been a severe pyelonephritis with loss of nephrons before operation, it is to be expected that this type of acidosis will develop quickly. Hyperchloræmic acidosis developing some years post-operatively could be due to a gradual destruction of renal parenchyma by hydronephrosis which is so common an event after ureteric transplantation.

No one technique has yet produced entirely satisfactory results in the human or in the dog. The inference is that the technique, with certain reservations, is irrelevant.

This is, in a sense, in agreement with the conclusions of Jacobs and Stirling (1952): "The nature of the lesion rather than the mode of technique was thus the major factor influencing immediate results." Our findings would agree with the conclusion of Leadbetter and Clarke (1954): "These observations make possible the observation that if renal function is normal prior to ureterosigmoidostomy and if a nearly normal functioning ureter results from operation there is little likelihood of troublesome hyperchloræmic acidosis."

The behaviour of the dog ureter corresponds to that observed clinically in man after uretero-intestinal anastomosis. Early dilatation of the dog ureter may retrogress after several weeks; Leadbetter and Clarke (1955) report similar findings; in this respect, if pyelograms are not carried out on the human till 4 weeks after operation a certain proportion of early dilated ureters will be missed. It was surprising that dogs with the Coffey I type of anastomosis were so well in spite of dilated ureters and pelves. This agrees with clinical reports:—

1. "Moderate degrees of dilatation may be consistent with a satisfactory clinical result in some cases" (Graves and Buddington, 1950).

2. "Hydronephrosis, on the other hand, probably develops over the course of months, and may not give rise to symptoms unless it becomes infected" (Grey Turner, 1946).

3. "Such sequels are liable to an aftermath of progressive renal deterioration from pyelonephritis with final uræmia, though this is not inevitable for there are patients alive for many years with marked bilateral dilatation, exhibited from the outset of their post-operative follow-up and nevertheless keep well" (Jacobs and Stirling, 1952).

The Nesbit operations, unfortunately, were performed during a cold spell in the winter months; these experiments require repeating on this account. Whether we can blame the cold spell for the poor post-operative results remains to be proved. Clinically, this used to be thought to be important; Grey Turner (1943) stated "... I would stress the wisdom of choosing the summer months for the ordeal and of keeping the children in hospital for a fortnight before operation". This perhaps will merely bring a smile to the face of the modern clinician! It is apparent, however, that the results of the Nesbit operation in man are not satisfactory either (Daniel, 1955).

The association between ascending infection and pyelonephritis is deeply ingrained in the mind of the clinical surgeon; most experimental evidence points against the association and favours bloodstream infection (Barrington and Wright, 1930; De Navasquez, 1950). Our results do not favour the view that infection ascends the ureter to produce acute pyelonephritis. Since our experiments were short-term, it was possible to distinguish between an acute infection resulting from the anastomoses and a chronic pre-existing pyelonephritis. This would hardly be possible in human kidneys so far as long-term results are concerned unless renal biopsy was used. The modern trend towards the use of ileal loops as a means of reducing ureteral reflux and pyelonephritis has also the aim of avoiding the alleged ascending infection. It will be interesting to see if the really long-term results justify the present enthusiasm. The results of Bricker, Butcher, and McAfee (1954) indicate that pyelonephritis and hydronephrosis may still develop in cases in whom the ureters have been anastomosed to isolated ileal loops.

We find ourselves in a large measure of agreement with the results of Weyrauch and Young (1952) although exact comparisons could not be made because of lack of individual documentation on their part. Since we experienced two very bad results with the direct implantation techniques, we join with them in condemning its use in man because of the possible dangers.

SUMMARY

There appears to be a definite relationship between canine nephritis and the persistence of dilatation of the ureter and renal pelvis after uretero-intestinal anastomosis; this is independent of the technique used. Since pyelonephitis is common in man, renal biopsy could reveal whether a similar correlation obtains in the human following ureterocolic anastomosis. If canine nephritis is severe, the chances of severe hydro-ureter and hydronephrosis developing after any type of anastomosis are high; and the chances of a superimposed acute pyelonephritis are also high. Ureters implanted high in the colon by the Coffey technique can give as good results as the Leadbetter operation; the latter gives no protection against the development of ureteric and renal pelvic dilatation if canine nephritis is a pre-operative condition. Despite certain anatomical differences between the ureter and the colon of man and dog, the results of transplanting ureters in dogs are valid for studying related problems in man since our results closely parallel those recently reached in the clinic after many years of empirical study.

Acknowledgements.—We are grateful to the Council of the Royal College of Surgeons for permission to carry out the work at the Buckston Browne Research Farm, Downe, Kent. The histological sections were prepared by Mr. Griffin and his staff; the photomicrographs are by the photographic department.

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THE PLASTIC REPLACEMENT OF SEVERED FLEXOR TENDONS OF THE FINGERS

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AN injury which involves the flexor tendons of the finger within the digital theca is a calamity, for although it is an apparently minor injury, at best the treatment is prolonged and complicated, at worst a significant percentage of cases fail ever again to recover a useful functioning finger.

Undoubtedly, results which were once universally bad have shown steady improvement over the past thirty years, largely due to the efforts of Bunnell (1944), Meyer (1938), Pulvertaft (1949), and many others, and although many excellent results can frequently be shown, the treatment is still far from satisfactory.

The technique which is to-day generally accepted as giving the most consistently satisfactory results is the replacement, with a free tendon-graft, of the cut flexor digitorum profundus tendon from the palm of the hand to the distal phalanx, together with the complete removal of the flexor digitorum sublimis tendon in this area.

For good results this technique requires skill, experience, great care, and the display of what Bunnell has described as "atraumatic surgery". However, an injury of the flexor tendons of the digits is a most common industrial and civilian accident, and a satisfactory surgical technique for its repair should provide the average surgeon with good promise of acceptable results. This, on the whole, is not the case with free tendon-grafting. The results obtained are to a large measure in a direct ratio to the skill and experience of the surgeon. The average practising surgeon seldom gets sufficient clinical material to gain skill and experience in this field, so that the majority of surgeons have found their results with this technique are far from satisfactory and amputation of the finger is often offered as the quickest and most practical treatment for a severed flexor tendon within the digital theca. However, failure with free tendon-grafting is not always the fault of the surgeon, for even in the most experienced hands results are not uniformly good. Successful cases do indeed give excellent results with almost full function, but, as shown by Kyle and Eyrebrook (1954), for no apparent reason a significant percentage of cases do not give these good results and marked limitation of movement results.

However, even apart from these aspects, the great length of time required for rehabilitation back to normal, after free tendon-grafting, is economically and socially a great disadvantage. According to Pulvertaft (1949), the patient in most cases is able to return to work four months after the operation, with recovery continuing for up to one year, given the intelligent co-operation and ability of the patient to continue exercises, physiotherapy, and supervision for this period. If two or more fingers are affected the invalidity periods are usually proportionately longer.

A further extremely common problem in digital tendon surgery, not yet completely answered by free tendon-grafting, is the severance of a flexor digitorum profundus tendon without associated damage to the sublimis tendon. Rank and Wakefield (1953) advise that great consideration should be given to an acceptance of the disability without any attempt at repair, for fear of interfering with the functioning sublimis unit. Sometimes arthrodesis of the terminal interphalangeal joint is advocated (Kyle and Eyrebrook, 1954) to overcome the serious disability of the absence of the functioning profundus tendon. Pulvertaft (1948) advises that if grafting of the profundus tendon be attempted, a thin graft should be used, and contrary to the usual practice, the sublimis

tendon should not be removed, but should be retained, so that if the result does not come up to expectation no harm has been done and the finger still has sublimis action.

The Digital Flexor Tendons and their Sheath.—Normal flexion of the fingers depends on the intact function of two muscle–tendon units; the flexor digitorum sublimis and the flexor digitorum profundus. These muscles arise in the forearm and their tendons pass distally through the hand to insertions in the fingers. The profundus tendons are inserted into the bases of the distal phalanges, and their function, as far as the fingers are concerned, is flexion of all the joints of the fingers. The sublimis tendons are inserted into the bases of the middle phalanges and their function, as far as the fingers are concerned, is mainly flexion of the proximal interphalangeal joints.

Absence of the sublimis unit in a finger is said to make the final clench of the finger weaker, but according to Pulvertaft (1948) in practice the power for ordinary use is usually found to be unaffected.

Soon after entering the finger, the sublimis tendon splits into two elements which embrace the profundus tendon, allowing it to pass on to its own more distal insertion into the distal phalanx. The tunnel formed by the two elements of the split sublimis tendon just allows the normal profundus tendon to slide through.

Surrounding the muscle–tendon units as far as the metacarpophalangeal joints is a loose, filmy, elastic medium, the paratenon. Beyond this the tendons pass through a relatively rigid inelastic covering, the osseofibrous flexor tunnel, which is differentiated into areas of lesser and greater thickening, the latter being concentrated over the phalanges to form a pulley system around which the tendons act. During the movement of full flexion of the finger the usual excursion of the profundus tendon through this system is 3·3 cm., whilst the sublimis tendon's excursion is 2·8 cm.

The Cut Digital Flexor Tendons and their Sheath.—When a tendon is divided in a sheath the muscle contracts and the tendon end, in an abortive attempt to reunite with its opposite end, attaches itself to anything in its neighbourhood. After repair, even if a meticulous and accurate tendon suture has been performed, similar adhesions form around the tendon.

Bunnell (1944), in an attempt to reduce these adhesions, advocated an "atraumatic technique" and developed the withdrawal suture, but no matter how meticulous the suture, some adhesions always form. In areas where the tendon is surrounded by paratenon, these fine adhesions, which form just as elsewhere, are not of the functional importance which they assume when they occur within the relatively rigid fibrous flexor sheaths of the fingers, where they seriously impair the normal excursion of the tendon. It is this fact which has made the flexor tendons of the finger in the area between the metacarpophalangeal joint and the proximal interphalangeal joint the most difficult situation for tendon repair. Clinically this area still sets a baffling problem to the restoration of normal function.

To meet these difficulties the technique of free tendon-grafting was devised, in an attempt to transfer the site of suture from the areas of the relatively rigid sheath to the areas of loose paratenon.

THE 'PLASTIC REPLACEMENT' OPERATION

Rationale.—The key to success in tendon repair in the finger lies in the total avoidance of adhesions around the tendon. On this rationale, a technique has been devised whereby the cut flexor tendon is replaced by a nylon filament covered with polythene tubing which functionally replaces the tendon between the distal phalanx and the wrist. Since adhesions cannot bind down this plastic 'tendon', no limitation of movement from this cause can occur. The technique therefore requires no special emphasis on 'atraumatic surgery'. Furthermore, since the dangers and problems of adhesions lose their importance, plastic replacement can in all cases, within the limits of the surgical principles of the primary suture of wounds, be performed as an emergency procedure at the time of the tendon's division. Minor degrees of infection, should they occur, do not lead to adhesions and tendon adherence, and can be successfully treated with full expectation of a functioning unit still emerging.

The problem of the divided profundus tendon in the presence of a functioning sublimis unit can also be overcome by plastic replacement of the profundus tendon, without danger of disturbance of sublimis function. The plastic simply by-passes the sublimis tendon, without interfering with it, the nylon and polythene sliding between the elements of the split sublimis tendon without any possibility of adherence developing between them.

Technique.—In practice it has been found quite satisfactory to perform the operation as an emergency procedure at the time of the injury, the usual contra-indications to any procedure more extensive than emergency surgery at the initial operation being observed. No hard and fast rules or time limits need be laid down. The appearance of the wound, the type of injury, its cleanliness or contamination, must all be taken into account. In all cases full antibiotic cover is given.

In dealing with the late case, that is at any time after skin healing of the laceration has occurred, it is important that a full range of the passive movements of the finger should be present before the operation is undertaken, since joint stiffness limits and delays recovery.

After general anæsthesia has been induced a pneumatic tourniquet is applied, since a bloodless field is essential for the operation. If the operation is performed at the time of the injury, thorough and meticulous cleansing of the wound, the hand, and the arm is then performed with a 1 per cent cetrimide solution. If the operation is performed after healing of the original laceration has occurred, preoperative skin preparation will already have been performed. A transverse incision which, as it reaches the mid-lateral line of the finger, is angled slightly distally (and proximally if necessary) is made in the distal interphalangeal flexion crease (*Fig.* 280).

The flaps so formed are carefully elevated, care being taken to avoid damaging the digital nerves. The termination of the flexor digitorum profundus

tendon as it passes to its insertion into the base of the distal phalanx is identified. At the level of this insertion a fine awl is carefully worked transversely through the base of the distal phalanx, a short mid-lateral incision being made on the opposite side of the finger to allow the point of the awl to emerge (*Fig.* 281). The awl is withdrawn and through the track bored by it a hypodermic needle is inserted. The size of the hypodermic needle should be such that the nylon to be used can just comfortably be threaded through its bore. A 36-in. length of undyed fishing nylon (breaking strain 37 lb.) is then threaded through the bore of the needle (*Fig.* 282) after which the needle is withdrawn over the nylon leaving the nylon threaded through the finger. Both ends of the nylon are then re-passed back through the skin incisions and brought out through the transverse incision in the distal flexor crease. The nylon now, instead of passing through the full thickness of the finger, only passes through the terminal phalanx, and the ends of the nylon protrude through the transverse incision in the flexor crease (*Figs.* 283, 284).

FIG. 280.—Illustrating the incisions for the plastic replacement of the flexor digitorum profundus tendon. The common site of division of the tendons, overlying the proximal phalanx is shown.

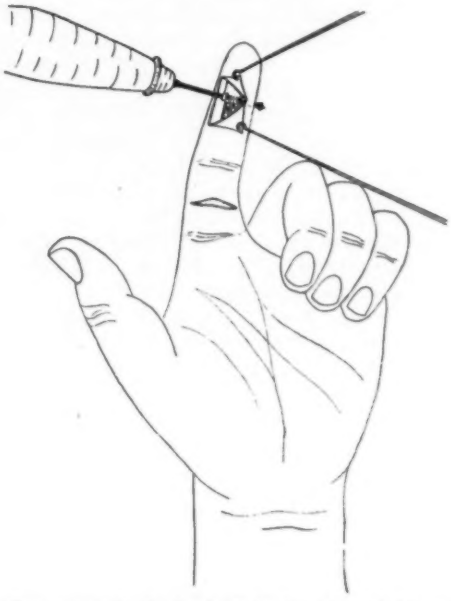

FIG. 281.—At the level of the insertion of the profundus tendon, a fine awl is worked transversely through the base of the distal phalanx, and a short mid-lateral incision is made on the opposite side of the finger for the point of the awl to emerge.

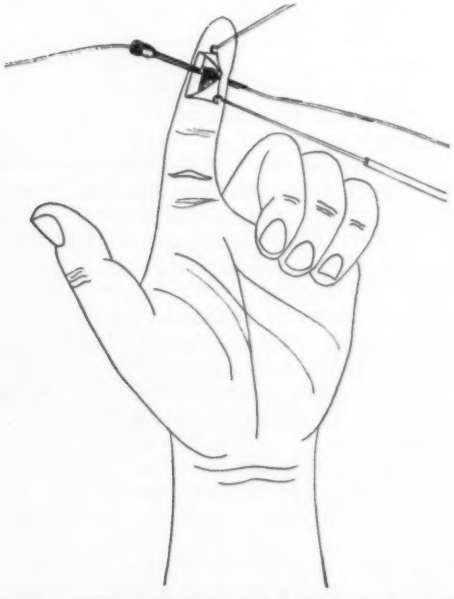

FIG. 282.—Through the track bored by the awl a hypodermic needle is passed, and a 36 in. length of undyed nylon (breaking strain 37 lb.) is threaded through the needle. The needle is then withdrawn over the nylon, leaving the nylon threaded through the finger.

The flexor tunnel, at the level of the insertion of the profundus tendon, is now incised and the distal segment of the cut profundus tendon is pulled out of the sheath and excised. A malleable silver probe is passed into and up the sheath, to the level of the division of the tendon and tendon-sheath, where the progress of the probe is often arrested.

If the operation is being performed at the time of injury, small retractors can now be inserted into the laceration, where the tendon is divided, and the edges of the laceration retracted. The tip of the probe can then usually be seen peeping out through the cut end of the tendon-sheath. Usually, without much difficulty, the opposite cut end of the sheath can be identified and the probe guided into it, after which the probe can usually be easily slid up the length of the sheath alongside the tendons completely through the hand and into the wrist, where the tip of the probe can once again be seen and felt as it presents almost under the skin (*Fig.* 283).

If the operation is being performed on a late case, that is once the original laceration has healed, the progress of the probe will be arrested at the site of the old division of the tendon and tendon-sheath by the adhesions and adherence of the sheath. With care, however, the probe can be guided through the

area of the adhesions to be followed by dilators which stretch the collapsed and adherent sheath to its normal diameter. Once the area of adhesions is passed, the probe can usually be slid down the sheath, through the hand, and on into the wrist.

FIG. 283.—The nylon ends have been passed back through the skin incisions and brought out through the transverse incisions in the distal flexor crease and threaded on the eye of a malleable silver probe which has been passed up the tendon-sheath and slid through the hand into the wrist. It can be seen presenting at the wrist.

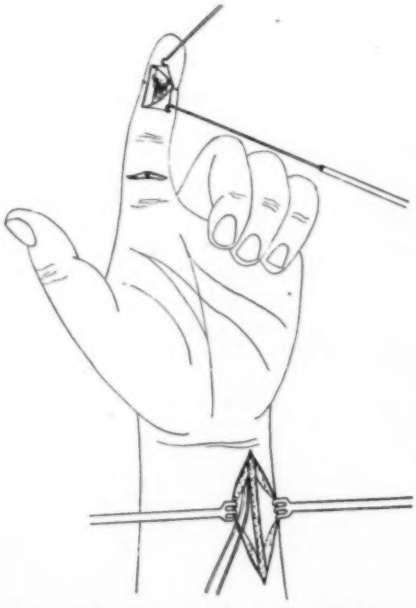

FIG. 285.—Through an incision at the wrist the tip of the probe and the flexor digitorum profundus tendon to the finger being operated upon are identified. The probe is then withdrawn into the wrist guiding the nylon filaments through into the wrist.

Once the tip of the probe has been passed through to the wrist a further 2-in. incision is made longitudinally at the wrist (*Fig.* 280) passing proximally from the transverse carpal crease in the line of the ulnar nerve, the incision being purposely placed more medial than required so that the possibility of adhesions between the flexor tendons and an overlying incision is avoided in the future. After incising the deep fascia, the flexor digitorum sublimis muscle with its tendons is identified and retracted laterally, whilst the flexor carpi ulnaris muscle and ulnar nerve are retracted medially exposing the flexor digitorum profundus tendons, amongst which the probe will be lying if it has been passed accurately through the tendon-sheath. The ends of the length of nylon,

FIG. 284.— In this patient a longitudinal laceration overlying the middle phalanx was extended along the distal interphalangeal crease forming a flap. The nylon ends which were passed through the base of the distal phalanx can be seen presenting through the laceration in the tendon-sheath.

which were threaded through the distal phalanx, are now threaded through the eye of the probe (*Fig.* 283) and the probe is drawn through into the wrist, thereby drawing the nylon through the tendon-sheath of the finger and hand right through into the wrist (*Fig.* 285). Occasionally, if the operation is performed at the time of the injury, instead of passing the probe the full distance from the tip of the finger to the wrist in one stage, it is easier to do so in two stages. As a first stage the probe and the nylon are passed out through the laceration, and as a second stage the probe is reinserted through the

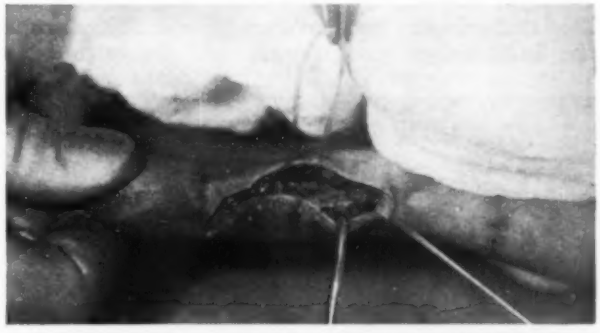

FIG. 286.—The probe has been inserted through the laceration and slid proximally up the tendon-sheath so that only the eye is visible. The nylon ends can be seen emerging from the cut distal end of the tendon-sheath and have been threaded through the eye of the probe.

laceration into the opposite end of the cut tendon sheath and only then slid completely through to the wrist (*Fig.* 286). If difficulty is experienced in passing the probe proximally through the tendon-sheath from the finger to the wrist, it may sometimes be more easily passed distally from the wrist to the finger. In this latter case, the eye of the probe instead of the tip should be passed first, so that the nylon filament can be threaded through it once it has been passed. Two polythene tubes (size 2, each having a bore of 1 mm.) are next slid

completely over the nylon filaments covering them up to the phalanx (*Figs.* 287, 288).

The tendons of the flexor digitorum profundus muscle are next examined. The profundus tendon to the finger being operated upon, or the tendon to

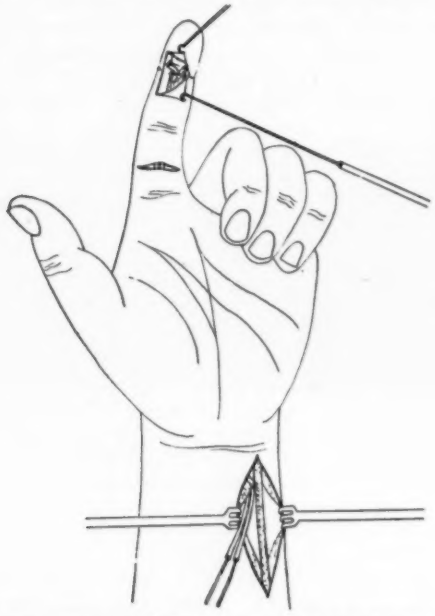

FIG. 287.—Two polythene tubes are slid completely over the nylon filaments, using them as guiding lines, so that the nylon is covered up to the phalanx.

the finger alongside the one being operated upon, is carefully identified and isolated. The nylon may be sutured to either one of these tendons. Traction is now applied to the nylon, so that the finger is flexed to its normal degree of flexion in relation to the other fingers. In the normal hand under anæsthesia, the fingers lie in a characteristic attitude with the little finger most flexed, and the succeeding

FIG. 289.—The normal hand under anæsthesia. The fingers lie in a characteristic attitude, with the little finger most flexed, and the succeeding fingers in lessening degrees of flexion.

fingers in lessening degrees of flexion (*Fig.* 289). With the finger held in this degree of flexion, the point at which the nylon filaments will eventually enter and join the profundus tendon is noted. The polythene tubing covering the nylon is divided at this point and the excess is removed. In this way the nylon strands are covered with polythene tubing, from the terminal phalanx to their junction into the tendon. The hypodermic needle (which was previously used for threading the nylon through the distal phalanx) is now passed obliquely through the profundus tendon selected, and one of the free ends of the nylon is passed through the bore of the needle, from the direction of its point (*Fig.* 290). Once the nylon is through the needle, the needle is withdrawn, leaving the nylon threaded through the tip of the tendon. A similar procedure is performed to thread

FIG. 288.—The polythene tubes have been threaded over the nylon filaments and slid up to the terminal phalanx. The excess polythene can be seen protruding at the wrist.

the other end of the nylon through the tendon (*Fig.* 291), and this procedure is then continued so that the two nylon ends are passed back and forth through the tendon, gradually working proximally till a length of $1\frac{1}{2}$–2 in. of the tendon have been interlaced by the nylon (*Fig.* 292). The needle is used to thread the nylon back and forth through the tendon, much in the manner of an atraumatic suture, thereby avoiding tearing the tendon. The length of the

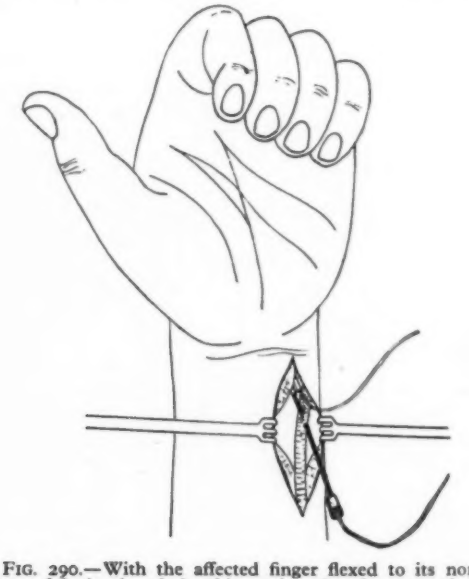

FIG. 290.—With the affected finger flexed to its normal degree of flexion in relationship to the other fingers as they lie relaxed under anæsthesia the excess polythene tubing is removed, and with a hypodermic needle the nylon is threaded obliquely through the tendon.

nylon and its covering of polythene between the finger and the tendon is next checked, so that the nylon is pulled just sufficiently through the tendon to hold the finger in its normal degree of flexion. It is extremely important that this is checked at this

stage before the nylon is tied and cut short. Once the nylon has been checked and found correct, it is tied with a triple knot. The ends of the knot are then laced once again through the tendon prior to being cut off, so that they are completely buried within the tendon (*Fig.* 292). The incision in the wrist, those in the finger and the original laceration, are all closed with interrupted non-absorbable sutures without drainage. Pressure dressings are applied to the wrist, the palm of the hand, and the affected finger. The tourniquet is then released.

After-care.—Full antibiotic cover is routinely maintained for seven days. The dressings are not

FIG. 291.—Both nylon filaments are threaded through the profundus tendon and drawn sufficiently through to flex the finger to its natural position of relaxation.

touched for ten days during which period movements are not actively encouraged, but are not prohibited. On the tenth day the stitches are removed, no dressing, beyond painting the finger with tinct. benz. co., usually being necessary. Active movements are then commenced and encouraged.

DISCUSSION

There are certain obvious questions that this technique raises.

Question 1: Are the nylon and polythene inert, or do they, or will they, cause immediate or delayed reactions either locally or generally?

Answer: Nylon is a generic term applied to a large family of related chemical compounds, and not to a single pure product, and therefore to discuss nylon one should know the exact chemical compound with which one is dealing. This is usually not possible, however, since commercial secrets prevent the detailed composition of individual products from becoming general knowledge. In practice, however, clinical and experimental results from various workers, who probably obtained the nylon with which they experimented from different supply houses, agree so closely that one can only conclude that the chemical differences in composition of the whole group are clinically of more apparent than real importance. Clinical trials of nylon have been reported by Stonham (1942), Haxton (1945), and Cumberland (1952). On the whole all report good tolerance of the tissues to nylon without marked foreign-body reaction around the nylon. Cumberland (1952) and Melick (1942) in experimental and clinical reports on the use of buried nylon for hernial repair have shown that in all cases tissue reaction was minimal and wound healing satisfactory. Kuhns and Potter (1951) embedded small pieces of nylon into the rectus sheath of rats and also into the denuded under-surface of patellæ in rabbits. Later, they performed a series of arthroplasties on the knee-joints of human patients, using a nylon membrane. No reaction to the nylon was observed.

There is also sufficient evidence to show that nylon is non-sensitizing. Jennes (1951) in testing employees in a nylon plant found no evidence of

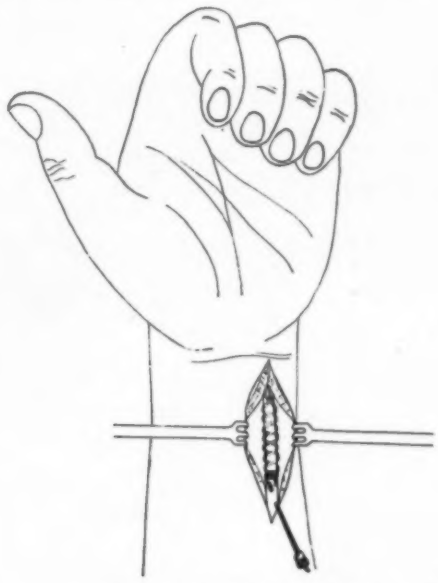

FIG. 292.—The nylon filaments are laced back and forth for 1½-2 in. up the tendon. Once its length has been checked and found correct, it is tied with a triple knot. The ends of the knot are then laced once again through the tendon prior to being cut off, so that they are completely buried within the tendon.

sensitization to nylon in any of the subjects tested even after many years of contact, although some of the subjects chosen were known sufferers from allergy, whilst others had known contact eczemas of various aetiological origins.

Finally, personal experiments support the wealth of evidence that nylon is relatively inert within the body. The plastic replacement operation has been performed experimentally in rabbits, a flexor tendon being replaced by nylon with the technique described above. The operation areas were re-examined at intervals of from one to eight months. Only mild degrees of reaction to the implanted nylon were noted. However, since nylon did show these mild signs of foreign-body reaction and since early clinical cases, where nylon alone was used, showed some limitation of movement as a result of peri-articular fibrosis, the nylon in later cases was covered with polythene. A long literature has accumulated on polythene, showing that in the tissues of the body it is probably completely inert. It causes no reaction provided it is pure and contains no contaminant (Brown, Grindlay, and Craig, 1947; Cooper, Robertson, Shea, and Dennis, 1949; Clagett, Grindlay, and Moersch, 1948; Donovan and Zimmerman, 1949; Ingraham, Alexander, and Matson, 1947; and Saybold, Grindlay, Pfentze, and Clagett, 1949). The impure variety contains a small percentage of dicetyl phosphate which has an irritating effect on the tissues, but all British-made polythene (which was used in this series) is of the

pure, non-irritating variety. Polythene tubing is obtainable in various diameters: size 2, which has a bore of 1 mm. and a wall 0·5 mm. thick, is the most convenient size for use in these cases. To replace the tendon with polythene only is, however, not practicable, since polythene has a relatively low breaking strain. Used, however, as a completely inert insulator to the mildly irritant but very strong nylon it is very satisfactory. If evidence should

FIG. 293.—Radiograph of the terminal phalanx of the forefinger 18 months after plastic replacement of the flexor digitorum profundus and sublimis tendons to that finger. The borehole through the base of the distal phalanx and the plastic 'tendon' in the tendon-sheath passing to it can be seen. No sign of erosion of the phalanx is evident.

appear that these plastics used within the body are irritant or carcinogenic over a long period, their use will have to be discontinued. The principle of tendon replacement could, however, be applied using metallic or other material.

Question 2: Can the fixation of the nylon, distally into the phalanx and proximally into the tendon, be strong and permanent enough to last the lifetime of a patient doing hard active digital work?

Answer: A catgut suture tied tightly around a bone leads to gradual erosion of the bone at the site and eventual fracture. It would seem probable therefore that the nylon, in passing through the terminal phalanx, with periodic tension due to muscular contractions imposed on it, would eventually cut out. This has not occurred, either experimentally or clinically, however, possibly because the tension of the nylon on the phalanx is never sufficient or prolonged enough to cause pressure erosion, or possibly because the direction of tension and compression on the phalanx is in alinement with its bony trabeculæ, for it now appears probable that compression of bone in the line of its trabeculæ does not have the same erosive effect which develops when the compression acts across the trabeculæ. The plastic replacement was performed on the flexor tendons of rabbits, the nylon being passed through the phalanx of a toe. The rabbits were subsequently examined at intervals of from one to eight months. In no case was there any tendency for the nylon to cut out; instead, the phalanx surrounding the bore hole had in most cases regenerated and the nylon was firmly incorporated in the bone. As for the fixation of the nylon into the tendon, in none of the experimental animals was there any evidence of loosening or slipping of the knot, or tearing out of the nylon; instead it had become further incorporated in the tendon and could be separated only by sharp dissection. Clinically, the operation has now been performed on 34 fingers, in a total of 22 patients, 8 patients having more than 1 finger involved. The longest follow-up is 2 years. In no case has the fixation of the nylon into the phalanx distally or into the tendon proximally loosened or presented any complication. Radiographs taken at intervals during periods of up to 18 months of constant hard digital work, have revealed no tendency for erosion of the phalanx to occur, or for the nylon to cut out (*Fig.* 293).

Question 3: Is the combined strength of the nylon and polythene comparable to the strength of the normal flexor tendon units, and if so, will this strength be maintained for the lifetime of a patient doing hard, active, digital work?

Answer: Cronkite (1935), in the course of a careful investigation into the tensile strength of human tendons, showed that it is not possible to establish a normal tensile strength for tendons since this varies so enormously. In fact, he found surprisingly, that the cross-section of a tendon is not necessarily a criterion of its tensile strength. By investigating a large number of certain tendons, however, he arrived at their average breaking strain. For the flexor digitorum sublimis and profundus tendons this was 220 lb. However, it is generally accepted (Mason, 1929, 1930; McMaster, 1932) that normal tendons are seldom if ever ruptured by either intrinsic or extrinsic force. They are either avulsed from the belly of the muscle or from the bone at its insertion, with or without an attached flake of bone. Since the tendon is therefore not the weakest link in the chain, it would appear more reasonable to test the muscle, tendon, and osseotendinous insertion as a unit, to find the breaking force of the unit. Fresh post-mortem specimens of the flexor digitorum profundus muscle together with its tendon and the phalanx into which the tendon was inserted were therefore tested for their breaking strain. The average breaking force was found to be 120 lb. In all cases the rupture occurred at the osseotendinous insertion into the phalanx with or without the avulsion of a flake of bone from the phalanx. The nylon and polythene to be used was then tested. The nylon used in this series was labelled by the manufacturer as having a 37 lb. breaking strain. In actual fact, when tested, the average breaking strain was 44 lb. Experimental specimens were then made from flexor digitorum profundus muscle–tendon–bone units, by replacing a section of the flexor digitorum profundus tendon with a loop of nylon covered in polythene passed through a tunnel bored in the base of the terminal phalanx, and sutured proximally to the tendon, in exactly the manner described for the plastic replacement technique. The breaking strains of these units were then tested. The average breaking strain

was found to be 115 lb. The rupture in each case occurred in the nylon's loop through the phalanx. Experimentally, therefore, after plastic replacement of the tendon, the unit appears to be of virtually comparable strength to the normal muscle–tendon–bone unit. Clinically, cases show as powerful a finger-clench and grip as is normally present, whilst patients frequently demonstrate their ability to perform single-finger weight-lifting as well as gripping and wielding hammers or using pliers and forceps.

FIG. 294.—Degree of flexion present 10 days after plastic replacement of the profundus tendon of the ring finger. The profundus and sublimis tendons had both been divided 4 months previously at the level of the proximal phalanx. The skin stitches can still be seen in position.

FIG. 295.—The same patient as in *Fig.* 294, illustrating the degree of extension present 10 days after the plastic replacement operation.

FIG. 296.—Degree of flexion present 14 days after plastic replacement of the profundus tendon of the little finger. The profundus and sublimis tendons had both been divided 6 months previously at the level of the metacarpophalangeal joint.

FIG. 297.—The same patient as in *Fig.* 296. Illustrating the degree of extension present 14 days after the plastic replacement operation.

FIG. 298.—Degree of flexion present 10 days after plastic replacement of the profundus tendon of the little finger, the operation having been performed as an emergency procedure 2 hr. after the patient had lacerated his finger on a knife. The tendons were divided at the level of the proximal interphalangeal joint. The skin stitches have not yet been removed.

FIG. 299.—The same patient as in *Fig.* 298. Illustrating the degree of extension present 10 days after the plastic replacement operation.

Question 4: Is the nylon or polythene liable to stretch when tension is placed upon it, especially when it is warm and wet as occurs when it is buried within the hand?

Answer: Neither nylon nor polythene deteriorate significantly with age and neither are affected by

being buried in animal or human tissue (Haxton, 1945). According to Stonham (1942) they may be stored in wet conditions for long periods without deterioration. In personal experiments on rabbits in which flexor tendons were replaced with nylon, no evidence of deterioration or loss of tensile strength of the nylon was observed, even after a period of eight months. Clinically, in no case has the accepted small degree of elasticity of either nylon or polythene caused any observable effects.

CONCLUSION

The present article is a preliminary report only on the plastic replacement of digital flexor tendons. The technique is relatively simple, and the results have appeared so encouraging that this first early report has appeared justified. The treatment of severed flexor tendons within the digital theca by plastic replacement appears to be both feasible and practicable, and at this early stage, appears consistently to give more than satisfactory results. The period of rehabilitation is incomparably more rapid than with free tendon-grafting (*Figs.* 294–299) whilst an extremely important factor which has emerged is that organized physiotherapy during rehabilitation is not essential. Moreover, after plastic replacement, the strict surveillance and the usual incessant encouragement to the patient to do his exercises repeatedly and frequently, lose much of their importance. Thus the intelligent co-operation and willingness of the patient is no longer as essential to a good result. Further experimental work and a complete report of clinical results will be published at a later date. For evaluation of late results, time alone will provide the answer. The principle of artificial tendons might however eventually be extended to the field of tendon transplantations and the rehabilitation of the paralysed. If artificial tendons can function along anatomical pathways there appears to be no reason why they should not function along artificial pathways. A tendon transplantation is commonly not practicable due to the anatomical lack of a suitable nearby tendon to reposition. If this limitation disappears there is no theoretical reason why a suitable muscle far removed from the paralysed area should not provide the motor power to that area via a long artificial tendon.

SUMMARY

The difficulties and disadvantages of free tendon-grafting of the profundus tendon as a method of treating divisions of the flexor tendons of the fingers within the digital theca are presented. The difficulties are mainly the special skill, experience, and great meticulousness that the technique demands, and the failure to obtain a good or satisfactory result in a significant percentage of cases even in expert hands. The length of time required for rehabilitation during which supervision and physiotherapy, together with the co-operation and willingness of the patient are necessary, and the difficulty of the treatment of a divided profundus tendon, near and in the presence of, a normal functioning sublimis unit. The anatomy, physiology, and pathology of the normal and the severed flexor tendon within the finger and hand are discussed, and it is shown that the key to success in tendon repair lies to a large extent in the total avoidance of adhesions around the tendon. On this rationale, a technique is described and illustrated in detail whereby severed flexor tendons in the digital theca are replaced by a double length of adequate strength nylon, covered by polythene, tubing which is inserted as a functioning unit between the distal phalanx, through which it is passed, and a profundus tendon at the wrist, to which it is firmly sutured, passing through the tendon-sheath *en route* from the finger to the wrist. The possible disadvantages and difficulties of the technique are discussed, namely the questions of the strength of the plastic, and of the junctions between it and the phalanx distally and the tendon proximally, and its inertness in the body. Experimental, clinical, and other evidence along these lines is presented.

Acknowledgements.—I should like to thank Dr. N. H. G. Cloete, the Medical Superintendent of the Groote Schuur Hospital, for permission to publish the reports of the cases, all of which were treated in that hospital. To Mr. Todt, of the Photographic Department, my thanks for the clinical photographs.

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THE INFLUENCE OF THE ADENOHYPOPHYSIS AND THE ADRENAL CORTEX ON GASTRIC SECRETION IN THE RAT

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Many factors regulate gastric secretion in health and disease. The influence of the number of secreting cells in the gastric mucosa, of vagal and gastrin stimulation, and of enterogastrone inhibition are well known. Other factors, which are less familiar, affect the secretion either directly or through one of these channels. The roles of the adenohypophysis and the adrenal cortex have only recently been recognized and are not yet fully understood.

Although they did not study gastric secretion, both Addison (1855) and Simmonds (1914, 1918) made observations suggesting that the adrenal and pituitary glands might influence the stomach. Anorexia and "irritability of the stomach" were described in Addison's disease and visceral splanchnomicria was noted in Simmonds' disease. Subsequently clinicians reported that achlorhydria occurred frequently in hypo-adrenalism (Rowntree and Snell, 1931) and even more commonly in hypopituitarism (Escamilla and Lisser, 1942). With the advent of cortisone and corticotrophin (ACTH) reports appeared that these hormones increased gastric acid and pepsin secretion and that peptic ulceration sometimes developed during their administration. Cushing's syndrome, in which there is an excessive production of adrenocortical hormones, is usually accompanied by gastric hypersecretion, and subtotal adrenalectomy restores the secretion to normal (Kyle, Logan, Neill, and Welbourn, 1956; Kyle and Welbourn, 1956).

In the rat cortisone does *not* increase gastric secretion and under certain conditions may even depress it (Welbourn and Code, 1953). Desoxycortone acetate (DOCA) may increase the volume and lower the acidity (Madden and Ramsburg, 1951). After bilateral adrenalectomy, secretion is diminished (Tuerkischer and Wertheimer, 1945; Madden and Ramsburg, 1951; Welbourn and Code, 1953), but it is not certain whether the volume or the acidity is the more affected. Cortisone, adrenocortical extract, and possibly DOCA restore the secretion after adrenalectomy (Tuerkischer and Wertheimer, 1945; Madden and Ramsburg, 1951; Welbourn and Code, 1953), but small doses of histamine do not (Tuerkischer and Wertheimer, 1945).

Apart from the observation that gastric pepsinogen is increased (Streeten, Hirschowitz, and Pollard, 1954), the effect of corticotrophin administration on gastric secretion in normal rats has not been reported. Secretion is reduced by hypophysectomy and can be partially restored by cortisone (Crafts and Walker, 1947; Baker and Abrams, 1954). Somatotrophin (growth hormone) has been found less effective (Baker and Abrams, 1955).

The experiments to be described were carried out in order to study systematically the influence of the adenohypophysis and adrenal cortex on gastric secretion in the rat. The general plan was to study gastric secretion after :—

a. The administration of hormones to intact animals.

b. Removal of the adrenal or pituitary glands.

c. The administration of hormones and drugs to adrenalectomized or hypophysectomized rats.

MATERIALS AND METHODS

White Wistar rats weighing 115–240 g. were used. In each experiment animals of similar weight and sex were allotted to corresponding test and control groups. Gastric secretion was measured by a modification of the pylorus-ligation technique of Shay, Komarov, Fels, Meranze, Gruenstein, and Siplet (1945). In this method advantage is taken of two characteristics of the rat : first, that secretion occurs at a constant rate, which is close to the maximal one, in the fasting state ; and secondly, that the rat cannot vomit, so that when the pylorus is occluded the secretions are retained in the stomach.

To prevent contamination of their gastric secretions by ingested food, fur, or fæces, the rats were isolated in individual cages (Bollman, 1948) for 48 hours before starting the gastric investigations. Some of the hypophysectomized rats, however, did not survive this period, and they and their controls were isolated for only 24 hours. All the animals were fasted during the isolation period but received fluid to drink—tap water for intact rats, 1 per cent saline after adrenalectomy, and 5 per cent glucose solution after hypophysectomy. At the end of this period each rat was weighed and this weight was used in the subsequent calculations.

The abdomen was then opened under light ether anæsthesia, and a ligature was tied gently around the pylorus. The abdomen was closed, and, after recovery from the anæsthetic, the rat was returned to its individual cage. Nothing further was given by mouth. This procedure was well tolerated and did not appear to cause any distress. Six hours later, after reopening the abdomen under anæsthesia, the abdominal œsophagus was clamped, the stomach was removed, and the rat killed. Shay, Sun, and Gruenstein (1954) have recently advocated washing out the stomach at the beginning of the experiment, and using a 4-hour period for the collection of secretions. In a controlled study (Kyle, 1956) no significant difference was found between the results obtained by this method and that used here.

After removal, the stomach was opened and its contents collected and centrifuged. The volumes of fluid and of debris were measured, and the acidity determined with a glass electrode *p*H meter. The few specimens that contained more than 0·3 ml. of debris were discarded. The stomach was finally examined with the naked eye and preserved.

Bilateral adrenalectomy was carried out through a midline dorsal incision just below the last ribs. The skin was drawn to each side in turn, the lumbar muscles were divided close to the erector spinæ mass, and the adrenal glands, lying in the fat at the upper poles of the kidneys, were exposed. The pedicle of each gland was crushed with a hæmostat and the gland avulsed, and the muscle and skin incisions

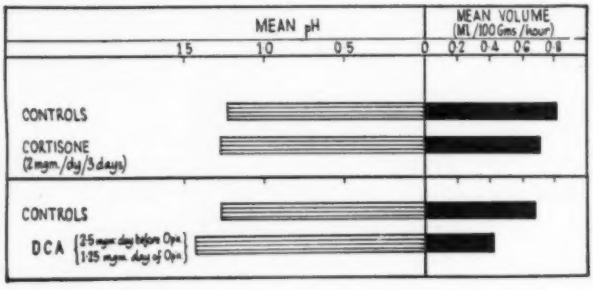

FIG. 300.—Effects of cortisone and of desoxycortone (DOCA) on gastric secretion.

were closed. When given 1 per cent saline to drink, adrenalectomized rats lived in good health for many months.

Hypophysectomy was performed by the technique described by Ingle and Griffith (1949). The rat was anæsthetized with ether and placed in the supine position. A median incision was made on the ventral aspect of the neck, and the infrahyoid muscles were split longitudinally on the right side just below the larynx. With intermittent retraction of the trachea to the left, the prevertebral muscles were scraped from the base of the skull. Using a No. 11 dental burr, a central hole was then drilled just cephalad to the basisphenoid–basi-occiput synchondrosis. The pinkish pituitary gland was seen at the bottom of the burr hole, and was removed by suction through a fine glass tube. The skin incision was then closed and the mouth and larynx wiped clear of mucus. The completeness of the hypophysectomy was assessed by inspection of the removed tissue, by the failure of the animals to gain weight, and by examination of the pituitary region when the animal was killed at the end of the experiment. After operation the animals were given 5 per cent glucose solution to drink.

To exclude the possibility of the operative trauma affecting gastric secretion, mock operations on the adrenal and pituitary glands were carried out in the same manner, except that the glands were not removed.

Hormones and drugs were given by intramuscular injection. The doses and times of their administration are stated in the following section. Except when otherwise indicated they were given during the period immediately preceding pyloric ligation.

RESULTS

The results are presented in tabular and in graphic form. The volume of gastric secretion in the rat is directly proportional to the weight of the animal (Madden, Ramsburg, and Hundley, 1951) and to the length of time during which the secretion is collected. It may therefore be conveniently expressed in ml. per 100 g. weight per hour. The mean volumes for the various groups of animals are represented in the figures by the black portions of the horizontal columns to the right of the vertical zero lines. The mean acidities, expressed in *p*H units,* are represented by the shaded portions to the left. Since the acidity varies inversely with the *p*H reading, the shift of a whole horizontal column to the right indicates that both the volume and the acidity of the secretion have increased. Conversely, when a whole column moves towards the left the secretion has diminished.

INFLUENCE OF THE ADRENAL CORTEX ON GASTRIC SECRETION

Neither cortisone nor DOCA increased gastric secretion in rats with intact adrenal glands. Cortisone acetate (2 mg. per day for 3 days) had no effect, while DOCA (2·5 mg. on the day before and 1·25 mg. at the time of pyloric ligation) *decreased* the volume and the acidity (*Fig.* 300 and *Table I*).

Table I.—EFFECTS OF CORTISONE AND OF DESOXYCORTONE (DOCA) ON GASTRIC SECRETION

GROUP	NO. OF RATS	*p*H			VOLUME (ml./100 g./hour)		
		Mean	S.D.	Statistical Analysis	Mean	S.D.	Statistical Analysis
Controls	6	1·23	0·06	$t = 1·08$, D.F. = 13, $0·3 > P > 0·2$	0·83	0·22	$t = 1·19$, D.F. = 13, $0·3 > P > 0·2$
Cortisone	9	1·28	0·09		0·71	0·17	
Controls	6	1·28	0·11	$t = 2·30$, D.F. = 14, $0·05 > P > 0·02$	0·67	0·17	$t = 3·22$, D.F. = 14, $0·01 > P > 0·001$
DOCA	10	1·42	0·14		0·41	0·15	

Bilateral adrenalectomy, 1–3 weeks previously, reduced both the volume and the acidity of the secretion (*Fig.* 301 and *Table II*). The mean volume was about one-half of that from intact rats and there was a marked reduction in acidity. Mock operations had no effect on secretion.

After adrenalectomy secretion was affected in different ways by cortisone, prednisone, DOCA, corticotrophin, and histamine. Cortisone acetate (10 mg. per day for 3 days) restored the acidity to normal and increased the volume to a level

* A 'mean *p*H' (which is derived from readings on an inverse logarithmic scale) may be criticized on the grounds that it is a highly artificial abstraction, but it is meaningful to those familiar with *p*H units and is amenable to statistical analysis. Moreover, *p*H meter readings are more accurate than titrations on small volumes of fluid.

significantly greater than normal. Prednisone, a potent synthetic analogue of cortisone (2·5 mg. per day for 3 days), restored the volume and the acidity, but did not cause hypersecretion. DOCA (in the dosage which depressed secretion in intact rats) restored the volume but not the acidity, and caused œdema to develop in the stomach wall and free fluid to collect in the peritoneal cavity. Corticotrophin (2 i.u. per day for 3 days) had no effect.

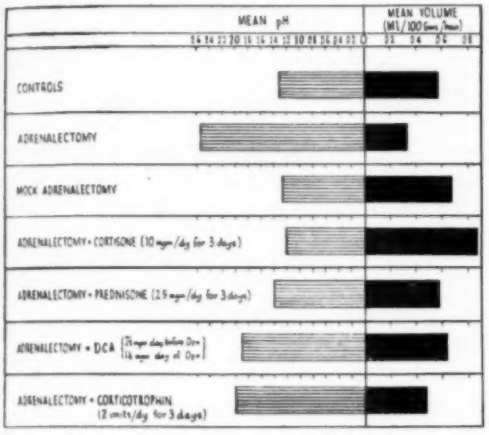

FIG. 301.—Effects of adrenalectomy and mock adrenalectomy, and of cortisone, prednisone, desoxycortone (DOCA), and corticotrophin after adrenalectomy on gastric secretion.

Histamine acid phosphate (5·5 mg. of histamine base per kg. in 5 divided doses following pyloric ligation) restored the volume and the acidity to normal (*Fig.* 302 and *Table III*). The larger doses (9–18 mg. per kg.), which are required to increase secretion in intact animals (Kyle, Welbourn, and Nevin, 1956), were toxic and frequently fatal after adrenalectomy. Smaller doses proved ineffective.

INFLUENCE OF THE ADENOHYPOPHYSIS ON GASTRIC SECRETION

Corticotrophin (2 i.u. per day for 4 days) and crude anterior pituitary extract (Parke, Davis, 0·4 ml. twice weekly for 6 weeks) had no effect on gastric secretion (*Fig.* 303 and *Table IV*).

Hypophysectomy, 1–5 weeks previously, profoundly reduced secretion (*Fig.* 304 and *Table V*). The mean volume was about one-third of that obtained from normal rats, and the acidity was markedly reduced. Mock hypophysectomy had no effect.

After removal of the pituitary, gastric secretion was restored by the administration of cortisone, corticotrophin, and somatotrophin. Cortisone (10 mg. per day for 3 days) restored the secretion to normal. (The volume was not increased above normal as it was when cortisone was given to adrenalectomized animals.) When corticotrophin was given daily from the time of hypophysectomy to the time of pyloric ligation (1 i.u. per day for 7 days) the secretion remained normal. (2 i.u. of corticotrophin per day, for 4 days, starting 4 days after hypophysectomy, had no effect.) Somatotrophin* (Armour, 1 mg. per day for 8 days, from the time of hypophysectomy) restored the secretion to normal.

Table II.—EFFECTS ON GASTRIC SECRETION OF ADRENALECTOMY AND MOCK ADRENALECTOMY, AND OF CORTISONE, PREDNISONE, DESOXYCORTONE (DOCA), AND CORTICOTROPHIN AFTER ADRENALECTOMY

GROUP	NO. OF RATS	pH		VOLUME (ml./100 g./hour)	
		Mean	S.D.	Mean	S.D.
1. Controls	21	1·31	0·26	0·59	0·22
2. Adrenalectomy	23	2·57	1·27	0·34	0·20
3. Mock adrenalectomy	9	1·26	0·06	0·65	0·21
4. Adrenalectomy and cortisone	5	1·23	0·09	0·89	0·17
5. Adrenalectomy and prednisone	6	1·40	0·20	0·58	0·09
6. Adrenalectomy and DOCA	8	1·87	0·59	0·64	0·24
7. Adrenalectomy and corticotrophin	6	2·05	0·55	0·45	0·17

Statistical Analysis

GROUPS COMPARED	DEGREES OF FREEDOM	DIFFERENCE BETWEEN MEANS	t	P	DIFFERENCE BETWEEN MEANS	t	P
1 *v.* 2	42	1·26	4·56	<0·001	0·25	3·85	P<0·001
1 *v.* 3	28	0·05	0·50	0·7>P>0·6	0·06	0·69	0·5>P>0·4
2 *v.* 4	26	1·34	2·37	0·05>P>0·02	0·55	5·72	P<0·001
1 *v.* 4	24	0·08	0·63	0·6>P>0·5	0·30	2·78	0·02>P>0·01
2 *v.* 5	27	1·17	1·17	0·05>P>0·02	0·24	2·85	0·01>P>0·001
1 *v.* 5	25	0·90	0·82	0·5>P>0·4	0·01	0·12	P>0·9
2 *v.* 6	29	0·70	1·52	0·2>P>0·1	0·30	3·52	0·01>P>0·001
2 *v.* 7	27	0·52	0·99	0·4>P>0·3	0·11	1·24	0·3>P>0·2

DISCUSSION

Gastric secretion in many species is influenced by circulating adrenocortical hormones, whose release is controlled by the adenohypophysis and, more remotely, by the hypothalamus. The administration of cortisone or of corticotrophin to man (Gray, Benson, Reifenstein, and Spiro, 1951), to dogs

* This preparation is said to be pure. The makers state that it is more likely to be contaminated by thyrotrophin than by corticotrophin.

(Zubiran, Kark, and Dragstedt, 1952 a; Zubiran, Kark, Montalbetti, Morel, and Dragstedt, 1952 b) and to monkeys (French, Longmire, Porter, and Movius, 1953) increases the secretion of hydrochloric acid by

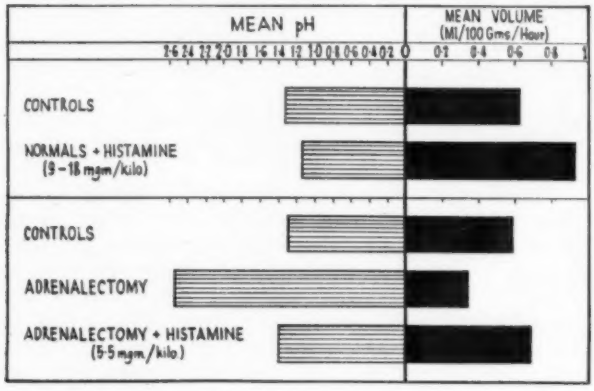

FIG. 302.—Effects of histamine on gastric secretion in rats with intact adrenals and after adrenalectomy.

the stomach, and stimulation of the posterior hypothalamus in monkeys has a similar effect (Porter, Movius, and French, 1953).

In the rat, however, the effect of the adrenocortical hormones appears to be different. All workers are agreed that bilateral total adrenalectomy reduces gastric secretion (Tuerkischer and Wertheimer, 1945; Madden and Ramsburg, 1951; Welbourn and Code, 1953) and our results show clearly that both the volume and the acidity are diminished. Medullectomy alone has no effect (Tuerkischer and Wertheimer, 1945), indicating that it is removal of the adrenal cortex which is responsible for the inhibition. Corticotrophin, however, has no effect on gastric secretion when the pituitary and adrenal glands are intact and cortisone increases secretion above the normal level only after adrenalectomy. This latter observation is new, but Welbourn and Code's (1953) data confirm it. It would appear, therefore, that the adrenal cortex of the rat produces some substance which prevents cortisone from stimulating the gastric mucosa, and this may possibly

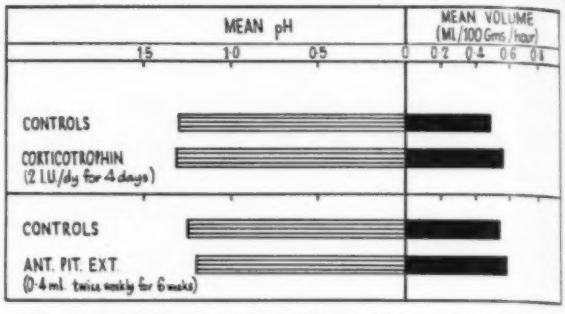
MEAN pH
MEAN VOLUME (Ml/100 Gms/Hour)
CONTROLS
CORTICOTROPHIN (2 I.U./dy for 4 days)
CONTROLS
ANT. PIT. EXT. (0·4 ml. twice weekly for 6 weeks)

FIG. 303.—Effects of corticotrophin and of anterior pituitary extract on gastric secretion.

be a mineralocorticoid such as aldosterone. The effects of the naturally occurring mineralocorticoids have not been studied in any species, but DOCA (which probably does not occur naturally) decreases the secretion of hydrochloric acid in the rat. We found that both the volume and the acidity were reduced, while Madden and Ramsburg (1951) found that the acidity was lowered although the volume of the gastric juice was increased. These authors stated that some of their rats were over-hydrated at the start of their experiment, and it is possible that the increase in volume which they observed after giving DOCA was the result of an increase in the volume of the extracellular fluid (Ledingham, 1954).

Table III.—EFFECTS OF HISTAMINE ON GASTRIC SECRETION IN RATS WITH INTACT ADRENALS AND AFTER ADRENALECTOMY

GROUP	NO. OF RATS	*p*H			VOLUME (ml./100 g./hour)		
		Mean	S.D.	Statistical Analysis	Mean	S.D.	Statistical Analysis
Controls	17	1·33	0·22	$t = 2·97$, D.F. = 34, $0·01 > P > 0·001$	0·63	0·22	$t = 3·79$, D.F. = 34, $P < 0·001$
Normals and histamine	19	1·14	0·14		0·93	0·24	
Controls (1)	21	1·31	0·26	(1) *v.* (3): $t = 0·72$, D.F. = 24, $0·5 > P > 0·4$	0·59	0·22	(1) *v.* (3): $t = 0·94$, D.F. = 24, $0·4 > P > 0·3$
Adrenalectomy (2)	23	2·57	1·25		0·34	0·20	
Adrenalectomy and histamine (3)	5	1·40	0·28	(2) *v.* (3): $t = 2·06$, D.F. = 26, $0·05 > P > 0·02$	0·69	0·21	(2) *v.* (3): $t = 3·58$, D.F. = 24, $0·01 > P > 0·001$

Table IV.—EFFECTS OF CORTICOTROPHIN AND OF ANTERIOR PITUITARY EXTRACT ON GASTRIC SECRETION

GROUP	NO. OF RATS	*p*H			VOLUME (ml./100 g./hour)		
		Mean	S.D.	Statistical Analysis	Mean	S.D.	Statistical Analysis
Controls	8	1·31	0·10	$t = 0·31$, D.F. = 17, $0·8 > P > 0·7$	0·60	0·24	$t = 0·06$, D.F. = 17, $P > 0·9$
Corticotrophin	11	1·33	0·10		0·59	0·14	
Controls	10	1·24	0·23	$t = 0·52$, D.F. = 18, $0·7 > P > 0·6$	0·54	0·33	$t = 0·32$, D.F. = 18, $0·8 > P > 0·7$
Anterior pituitary extract	10	1·20	0·07		0·58	0·23	

We observed a similar effect from giving DOCA after adrenalectomy when we found evidence of a general accumulation of fluid in the body tissues.

Hypophysectomy in the rat depresses the gastric secretion to a greater extent than adrenalectomy, but the reason for this is not clear. On the one hand it has been observed that removal of the adrenals, the thyroid, and the gonads produces an effect similar to that of removal of the pituitary (Abrams and Baker, 1954), while on the other both corticotrophin and cortisone restore secretion completely after hypophysectomy. Cortisone, however, does not cause a supranormal secretion as it does after adrenalectomy, and it may be that it can only do so when the thyroid and gonads are being normally stimulated by the anterior pituitary. Another possibility is that there is a basal secretion of mineralocorticoid by the suprarenal cortex (Singer and Stack-Dunne, 1955) and that this prevents cortisone from exerting its full effect. The action of the posterior pituitary gland on gastric secretion in the rat is unknown, but in dogs it has no effect (Atkinson and Ivy, 1938) and in rabbits and cats the vasopressor fraction of its extract inhibits secretion (Cutting, Dodds, Noble, and Williams, 1937).

It is not altogether surprising that the effects of the anterior pituitary and adrenocortical hormones on gastric secretion in the rat are different from those found in other species. In the first place, the adrenal is not so vital an organ in the rat as it is in higher animals, for the rat can be maintained in good health after adrenalectomy simply by giving it normal saline to drink; most higher animals require adrenocortical hormones. Secondly, the secretions of the adrenal cortex of the rat are different from those of other species (Hechter and Pincus, 1954). While hydrocortisone, which has an effect on gastric secretion similar to that of cortisone, is the main glucocorticoid in man and the dog, corticosterone, which does *not* increase gastric secretion (measured by uropepsin excretion) in man (Wolfson and Timmis, 1955), is the main glucocorticoid in the rat.

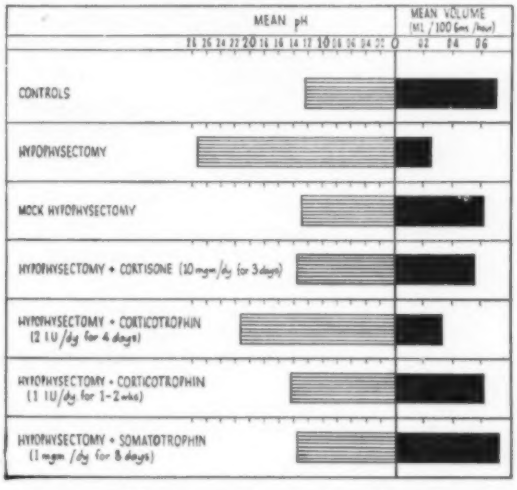
MEAN pH
MEAN VOLUME
CONTROLS
HYPOPHYSECTOMY
MOCK HYPOPHYSECTOMY
HYPOPHYSECTOMY + CORTISONE (10 mgm/day for 3 days)
HYPOPHYSECTOMY + CORTICOTROPHIN (2 I.U/day for 4 days)
HYPOPHYSECTOMY + CORTICOTROPHIN (1 I.U/day for 1-2 wks)
HYPOPHYSECTOMY + SOMATOTROPHIN (1 mgm /day for 8 days)

FIG. 304.—Effects on gastric secretion of hypophysectomy and mock hypophysectomy and of cortisone, corticotrophin, and somatotrophin after hypophysectomy.

The mechanisms involved in the stimulation or depression of gastric secretion by altering the hormonal environment of the secretory cells have been investigated very little, but several points require discussion :—

1. Atrophy of the gastric mucosa has been observed several weeks or months after hypophysectomy in cats (Haeger, Jacobsohn, and Kahlson,

Table V.—EFFECTS ON GASTRIC SECRETION OF HYPOPHYSECTOMY AND MOCK HYPOPHYSECTOMY, AND OF CORTISONE, CORTICOTROPHIN, AND SOMATOTROPHIN AFTER HYPOPHYSECTOMY

GROUP	NO. OF RATS	*p*H		VOLUME (ml./100 g./hr.)	
		Mean	S.D.	Mean	S.D.
1. Controls	17	1·27	0·16	0·71	0·24
2. Hypophysectomy	15	2·73	1·60	0·26	0·12
3. Mock hypophysectomy	8	1·27	0·16	0·60	0·07
4. Hypophysectomy + cortisone	8	1·34	0·16	0·56	0·12
5. Hypophysectomy + corticotrophin for 4 days	6	2·12	0·73	0·33	0·18
6. Hypophysectomy + corticotrophin for 1–2 weeks	9	1·43	0·25	0·61	0·15
7. Hypophysectomy + somatotrophin	5	1·35	0·21	0·71	0·20

Statistical Analysis

GROUPS COMPARED	DEGREES OF FREEDOM	DIFFERENCE BETWEEN MEANS	t	P	DIFFERENCE BETWEEN MEANS	t	P
1 *v.* 2	30	1·46	3·77	$P<0.001$	0·45	6·54	$P<0.001$
1 *v.* 3	23	0·00	—	—	0·11	1·25	$0.3>P>0.2$
1 *v.* 4	23	0·07	1·12	$0.3>P>0.2$	0·15	1·68	$0.2>P>0.1$
2 *v.* 4	21	1·39	2·43	$0.05>P>0.02$	0·30	5·69	$P<0.001$
2 *v.* 5	19	0·61	0·82	$0.5>P>0.4$	0·07	1·01	$0.4>P>0.3$
2 *v.* 6	22	1·30	2·41	$0.05>P>0.02$	0·35	6·28	$P<0.001$
2 *v.* 7	18	1·38	1·90	$0.1>P>0.05$*	0·45	6·11	$P<0.001$

* The fact that this difference does not quite reach the 5 per cent level of significance is due to the small number of animals (5) in Group 7 and to the high standard deviation in Group 2. The ranges of readings, however, did not overlap and there can be little doubt that the difference is real.

1953) and in rats (Friedman, 1953), and in the latter species the atrophy can be prevented by somatotrophin (Simpson, Evans, and Li, 1949). This atrophy may be the cause of the decrease in gastric secretion. However, we found no alteration in the height of the gastric mucosa and no obvious change in the number of parietal cells present in our animals at the time of our experiments (Kyle, 1956). This suggests that hypophysectomy inhibits secretion and that cortisone, corticotrophin, and somatotrophin restore it by some 'physiological' process and not by an 'anatomical' one. It should, however, be noted that degenerative changes, affecting the zymogen cells (which secrete pepsinogen) more than the parietal cells (which secrete acid), have been found by special staining techniques within a few days of hypophysectomy or adrenalectomy (Baker and Bridgman, 1954; Baker and Abrams, 1954), and adrenocortical hormones may be necessary for the enzyme reactions that take place within these specialized cells.

2. The actions of corticotrophin and of cortisone appear to be independent of vagal stimuli, for both hormones increase gastric secretion in man (Gray, Benson, Reifenstein, and Ramsey, 1952), the monkey (French, Longmire, Porter, and Movius, 1953), and the dog (Zubiran and associates, 1952 a, b) after vagotomy. However, cortisone does not restore secretion after vagotomy in the rat when the pituitary and adrenal glands are intact (Welbourn, unpublished data).

3. The action of histamine (which may represent the 'final common path' of all stimuli affecting the parietal cells—Code, 1955) is not dependent on the presence of the adrenocortical hormones, for histamine restores secretion after adrenalectomy.

4. A raised blood-urea has been shown to depress gastric secretion in man (Fitzgerald and Murphy, 1950) and it is possible that uræmia might influence the secretion after adrenalectomy. Our rats, however, maintained on normal saline, had normal concentrations of urea in the blood (Kyle, 1956).

In conclusion it is clear that the hormones of the adenohypophysis and adrenal cortex are essential for maintaining normal gastric secretion. There are, however, important differences between their actions in the rat and in other species, including man.

SUMMARY

1. An investigation of the influence of the adenohypophysis and the adrenal cortex on gastric secretion in the pylorus-ligated rat was undertaken.

2. The administration of cortisone, corticotrophin, or anterior pituitary extract did not increase gastric secretion in normal rats. Desoxycortone reduced secretion.

3. Adrenalectomy reduced secretion, after which cortisone restored the acidity to normal and increased the volume of secretion above normal. Prednisone restored the acidity and the volume to normal. Desoxycortone restored the volume of secretion, but not its acidity, and produced œdema of the stomach wall and ascites.

4. Histamine restored secretion in adrenalectomized rats, the effective dosage being only one-third of that required to increase secretion in normal animals.

5. Hypophysectomy had an even more marked inhibitory effect on gastric secretion than adrenalectomy. Secretion was restored by cortisone, corticotrophin, or somatotrophin.

6. The diminution in secretion caused by removal of the pituitary or adrenal glands was not due to gross atrophy of the gastric mucosa, or to alteration of the blood-urea level.

7. There are differences between the actions of adrenocortical hormones on gastric secretion in the rat and those reported in other species, including man.

Acknowledgements.—We wish to thank the Northern Ireland Hospitals Authority for the cortisone and corticotrophin, Roussel Laboratories Ltd. for prednisone, Parke, Davis & Co. for anterior pituitary extract, and Armour Laboratories for the somatotrophin. We are indebted to Mr. G. A. Smith and Mr. R. G. Wood for the illustrations, to Dr. E. A. Cheeseman for his advice on the statistical analyses, and to Miss R. Orr for secretarial assistance.

James Kyle was in receipt of the Linen Industrial Research Grant.

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LIGATION OF BOTH THE CŒLIAC AXIS AND SUPERIOR MESENTERIC ARTERY WITH SURVIVAL OF THE PATIENT

BY C. G. ROB AND KENNETH OWEN

Hâtez-vous lentement, et, sans perdre courage,
Vingt fois sur le métier remettez votre ouvrage :
Polissez-le sans cesse et le repolissez ;
Ajoutez quelquefois, et souvent effacez.—
" L'Art Poétique " (BOILEAU).

THIS quotation was used by Belou (1915) in his monograph on the biliary ducts and cystic artery and is a wise injunction to anyone describing the problem of hepatic arterial supply. This report is of a case which suggests further adjustments to earlier views on this subject.

Surgical opinion has varied widely as to the importance of the hepatic arterial supply and the risks of hepatic artery interruption. The first ligation of this vessel was performed by Simon de Metz (1828) on doves. He found that this produced no alteration in the flow of bile. For obvious reasons there are few published reports of the effects of accidental hepatic artery damage in man, but it is widely taught that the risks of liver necrosis are high and this is reinforced by the experimental work of Haberer (1905) and Narath (1916), both of whom cite many other workers' results. Haberer (1905) first drew attention to the site of ligation in dogs. If this were distal to the gastroduodenal artery severe necrosis followed, but if proximal the collateral supply from the superior mesenteric was adequate for liver-cell survival. A similar result was obtained in rabbits by Cameron and Mayes (1930).

The difficulties of applying the experimental results to man have been shown by Childs (1954), who demonstrated great species differences between the susceptibility of the dog, the macaca monkey, and man to hepatic artery interruption. Markowitz, Rappaport, and Scott (1949) had previously shown that invasion of the liver by anaerobes was a contributory cause of death in dogs and could be prevented by administering penicillin. Brunschwig (1953) emphasizes the differences between dog and man, stating that the canine liver is heavily infected with anaerobic organisms whereas the human liver is sterile.

In man the hepatic artery was successfully ligated distal to the origin of the gastroduodenal by Hans Kehr (1903), and similar successes are recorded by Sudeck (1919) and Colmers (1921). Two cases of

FIG. 305.—Aneurysm of upper abdominal aorta.

hepatic aneurysm were recorded by Grant, Fitts, and Ravdin (1950) with ligation of the hepatic artery but both were fatal. Graham and Cannell (1933) reported a case of accidental ligation of the hepatic artery and reviewed the literature of 27 such cases. They concluded that hepatic artery ligation, although

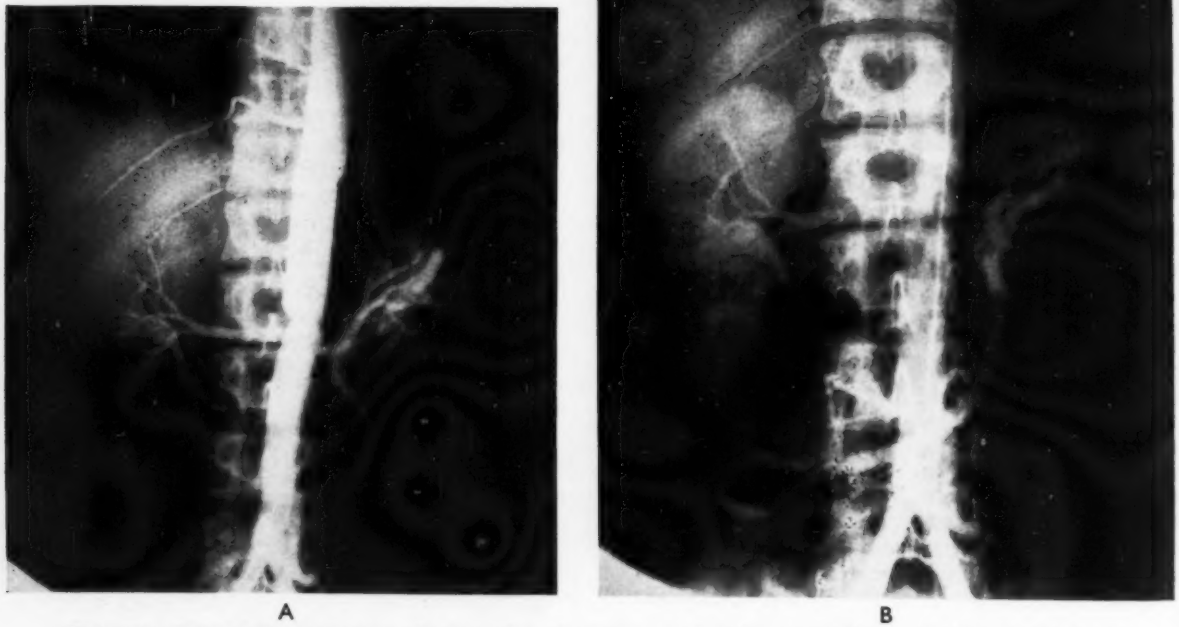
potentially serious, was not necessarily fatal. In 1947 Rienhoff ligated the hepatic artery distal to the gastroduodenal in the treatment of portal hypertension, and in 1951 he reported 6 successful cases.

FIG. 306.—Divided ends of aorta, with clamps on both renal arteries, after resection of aneurysm. The other clamps are on the aorta itself and an intercostal artery.

Many other surgeons have used this procedure but with less influence on the disease.

Appleby (1953) emphasizes the adequate collateral circulation to the liver from the superior mesenteric artery by way of the gastroduodenal and advocates the division of the cœliac axis in radical gastrectomy for carcinoma of the stomach. He records 13 cases with no demonstrable disturbance of liver function. The large part played by the superior mesenteric artery in maintaining a collateral circulation to the liver is stressed by Michels (1953, 1955) and by Appleby (1953). The present case is of great interest in that the three branches of the cœliac axis and the superior mesenteric artery were interrupted at their origin without demonstrable effect upon the patient or his liver function.

FIG. 307.—Polyvinyl alcohol sponge tube replacing upper abdominal aorta. Note the left renal vein just below the distal anastomoses.



A B

FIG. 308.—Post-operative aortogram after resection of aneurysm and replacement with a polyvinyl alcohol implant showing hypertrophic inferior mesenteric artery and enlarged lower intercostal arteries. Note the absence of both the cœliac axis and superior mesenteric arteries.

CASE REPORT

H. T., a man aged 35, was admitted to King's College Hospital on June 5, 1955, complaining of heartburn after meals for one year, epigastric pain, and pain in the left hypochondrium for six months. Shortly before admission his pain had radiated to his back. In 1944 in Trinidad he developed a penile ulcer and inguinal abscess and was treated for lymphogranuloma inguinale, and on returning to England had further treatment. On examination at

King's College Hospital he was found to have an upper abdominal aneurysm. His W.R. and Kahn test were positive. He was treated with 1 million units of penicillin a day for 8 days.

Three months later a laparotomy was performed by Mr. Harold Edwards, following aortography which had revealed a saccular swelling of the abdominal aorta from the level of T.12 to L.3 (*Fig.* 305). The aneurysm was seen to be presenting through the lesser omentum. The splenic artery was opened and a cannula was inserted through this opening into the aneurysm, which was wired. The patient made a straightforward recovery from this operation, but when seen again in November, 1955, his aneurysm appeared to be enlarging and he was referred to us at St. Mary's Hospital.

A second operation (C. G. R. and K. O.) was performed at St. Mary's Hospital on January 11, 1956, under hypothermic anæsthesia (Dr. Alan Cheatle), his temperature being reduced by means of external cooling to 28° C. A left thoraco-abdominal incision was made and the aneurysm approached by reflecting forward the spleen, stomach, and tail and body of the pancreas. It was found to extend from just below the diaphragm to the renal arteries. The three branches of the cœliac axis were found arising from the front of the aneurysm while the superior mesenteric artery arose from its lower part. Preparation had been made to graft these vessels but they were each incised in turn and there was found to be no flow from the proximal end so that it was felt safe to ligate all four arteries, as their origin had presumably been thrombosed for some time with no apparent effort on the upper abdominal organs. The aneurysm was removed after clamps had been applied to the aorta above and below and to both renal arteries (*Fig.* 306). A tubular prosthesis of polyvinyl alcohol sponge (Prosthex) was sutured into position (*Fig.* 307). The clamps were in position for 96 minutes.

The patient made a straightforward post-operative recovery with no clinical evidence of any disability from the loss of his upper abdominal blood-supply or the clamping of the renal arteries for 96 minutes.

Liver function tests were performed on January 23, 1956. The total proteins were 6·4 per cent (albumin 3·8 per cent; globulin 2·6 per cent). Serum-bilirubin, alkaline phosphatase, and thymol turbidity readings were within the normal laboratory range.

A post-operative aortogram was performed on January 27 and showed no branches of the aorta between the eleventh intercostal artery and the renal arteries (*Fig.* 308 A). The inferior mesenteric artery was hypertrophied with a large ascending left colic branch and appeared to be the sole abdominal visceral supply (*Fig.* 308 B).

DISCUSSION

The maintenance of such a good collateral arterial supply to the upper abdominal organs without any clinical sign of hepatic insufficiency may have been aided by the occlusion of the cœliac axis branches and superior mesenteric occurring slowly and in stages. The first similar case to be reported was described by Chiene in 1869. His patient was a woman of 65 with an abdominal aneurysm who had died of another cause. It was found on post-mortem dissection that she had a long-standing thrombosis of the cœliac axis, superior mesenteric artery, and inferior mesenteric artery. She had developed an adequate circulation to the viscera from her parietal branches. Livierato, Vagliano, and Dervanaga (1935) report sudden complete deprivation of the hepatic arterial supply to be fatal to the experimental animal, but if the operation is done in stages the animal survives. This was confirmed by Huggins and Post (1937).

The sources of a collateral supply to the liver have been described admirably by Michels (1953, 1955) in an exhaustive study based on 200 dissections. Of the possibilities quoted by Michels it would seem from the aortogram that the main supply in this case is derived from the inferior mesenteric artery, through the marginal artery and the middle colic artery, to the superior mesenteric artery. From this vessel blood may reach the gastroduodenal artery by way of the inferior pancreaticoduodenal or through the transverse pancreatic artery and the left gastro-epiploic vessel. There are no other large vessels to be seen on the aortogram, except for slight enlargement of the lower right intercostals, and at operation no aortic branches were left between the diaphragm and the renal arteries. Some proportion of arterial blood may, however, be reaching the liver by the following routes :—

1. From the aorta through branches of the inferior phrenic arteries entering the liver through the bare area.
2. From the internal mammary artery by twigs from the superior phrenic arteries.
3. From the internal mammary artery through vessels travelling in the falciform ligament.
4. From intercostal or lumbar arteries through small branches reaching the liver posteriorly.

SUMMARY

1. The effects of hepatic artery interruption are discussed.

2. A case is described of a syphilitic aneurysm of the upper abdominal aorta which had produced thrombosis of the cœliac axis branches and the superior mesenteric artery. During the resection of the aneurysm and its replacement with a tubular graft these vessels were ligated with no detectable effect on the liver or other upper abdominal organs.

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OBSERVATIONS ON A CASE OF EXTERNAL PANCREATIC FISTULA IN MAN

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OWING to the rarity of opportunities for quantitative collection of pancreatic external secretion uncontaminated by bile or intestinal juices and the fact that patients with external pancreatic fistulæ can seldom be adapted to controlled conditions of study, observations on human pancreatic function remain fragmentary and often of dubious physiological validity.

An opportunity to make such a study was afforded by the following case.

CASE REPORT

HISTORY.—A 47-year-old male was admitted to hospital on account of epigastric pain and vomiting. For twenty years he had had symptoms of duodenal ulcer and an ulcer had been demonstrated radiologically five years after the onset of symptoms. Remissions had become progressively less frequent and of shorter duration and he was losing a great deal of time from his work. On admission he was in good general condition. There was moderate tenderness on deep palpation in the epigastrium and gastric succussion was present.

OPERATION.—There was an active posterior duodenal ulcer and early pyloric stenosis. The duodenum was mobilized beyond the ulcer, which was densely adherent to the pancreas to the right of the gastroduodenal artery. During the course of this dissection the capsule was removed from the anterosuperior aspect of the head of the pancreas. There did not appear to have been any damage to pancreatic parenchyma; a duct was not seen in the tissue ligated and divided during the dissection, nor was there any collection of fluid in this area either during the mobilization of the duodenum or subsequently. The operation was completed as a radical (five-sixths) partial gastrectomy of the Polya type, continuity being re-established by a retrocolic anastomosis 4 cm. long adjacent to the greater curvature of the gastric remnant. Before the abdomen was closed a rubber-tube drain was passed down to the region of the duodenal stump.

AFTER-COURSE.—The following morning the patient was suffering from more pain than is usual; his temperature remained at about 101° F. during this and the second post-operative day. On the second day the patient looked toxic and for the first time complained of pain in the back. There had not been any vomiting and occasional bowel-sounds could be heard. There were no clinical signs in the chest or abdomen to explain the picture. The drainage tube yielded less than 15 ml. of serous fluid over the first 48 hours.

On the morning of the third day after operation the tube was found to be discharging freely a colourless opalescent fluid. The patient said he felt much better, the back pain having subsided. From this time onward the patient's general condition improved rapidly. His fever subsided gradually over the following week, by the end of which he had a voracious appetite; but the drain continued to discharge copious amounts of pure pancreatic juice. During the first 24 hours of the discharge 2400 ml. were collected, and drainage continued thereafter at a daily level which varied from less than 300 ml. to over 1700 ml. Protection of the skin of the abdominal wall was not necessary because leakage did not occur around the abdominal drain; moreover tryptic activity was absent from the discharge in the early weeks when the pancreatic juice was sterile. The continuing loss of electrolytes presented a more urgent problem. In view of the patient's good general condition, control of his electrolyte balance was entirely by mouth. Water at his bedside was replaced by fruit-juice diluted with half-strength Darrow's solution. At first this fluid was accepted reluctantly, but soon the patient not only tolerated but came to enjoy the flavour of his fruit drink, and half-strength Darrow's solution was given over the subsequent two months. During the whole of this time his blood-electrolyte pattern never departed significantly from normal. The third clinical problem was the replacement of pancreatic enzymes. Although it would have been quite simple to feed the patient with his own pancreatic juice by nasal tube, it was decided to employ

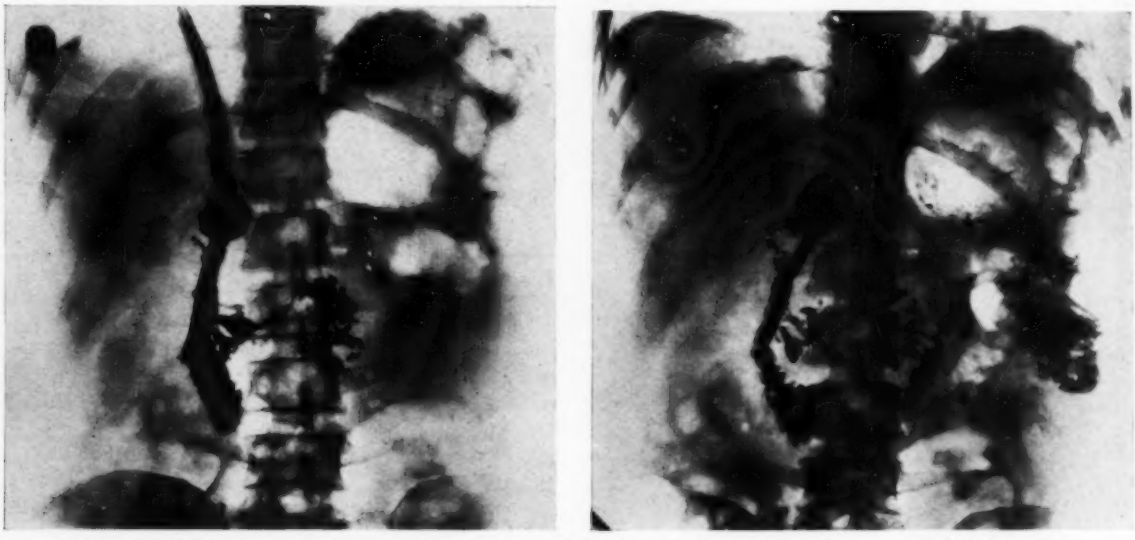

FIG. 309.—Radiographs of abdomen taken 2 min. and 10 min. after the injection of 10 ml. of lipiodol into the drainage-tube.

triple-strength pancreatin (Lilly) orally, so as to secure the pancreatic juice.

In view of the persistence of the fistula and the ease with which the patient's general condition was maintained, it was considered justifiable with the patient's full co-operation to carry out a series of tests while spontaneous closure of the fistula was awaited. This took place ten weeks after operation.

Preliminary Observations.—

1. *Site of Fistula.*—To establish the source of the fistula, under fluoroscopic control lipiodol was gently injected into the drainage-tube. In all, 10 ml. of lipiodol were introduced without discomfort to the patient. It was confirmed that the fistula arose from the head of the pancreas (*Fig.* 309). Although two distinct channels in the head of the pancreas were filled with opaque medium, it could not be demonstrated with certainty that the fistula arose from the more cephalad of the two ducts as was anticipated on anatomical grounds; such a fistula is at least potentially a total pancreatic fistula.

2. *Extent of Fistula.*—Less than one minute after the injection of lipiodol was started, a small amount of the medium was observed to pass into the duodenum; therefore it could not be assumed that all the pancreatic secretion which passed along the injured duct would flow through the fistula. Moreover, although the contrast radiographs and the volume of discharge from the fistula left no doubt that the major pancreatic duct had been damaged, and although the immediate post-operative course suggested that no alternative channel was available, the possibility remained that a lesser duct might continue to discharge into the bowel the secretion from a small part of the pancreatic head. Repeated tests of the upper jejunal contents for tryptic activity showed this to be present only intermittently. There was, in addition, gross disturbance of both splitting and

Table I.—Fæcal Fat Analysis

Post-operative Day	Total Fat Percentage of Dry Weight	Split Fat Percentage of Total Fat	Unsplit Fat Percentage of Total Fat	Therapy and Clinical State
32	44	27	73	Pancreatin 5 g. daily by mouth
34	49	18	82	
48	60	10	90	No enzyme replacement
69	45	15	85	Fistula closing
79	21	81	19	Fistula closed

absorption of fat in the bowel (*Table I*). Therefore it is likely that for considerable periods the loss of pancreatic juice through the fistula was complete.

3. *Functional State of the Pancreas.*—The radiological study showed the pancreatic duct system to be grossly dilated (*Fig.* 309). This may have been a recent development because the main pancreatic duct had undoubtedly been occluded by ligature for more than 48 hours; on the other hand, it is possible that the dilatation was of longer standing, being related to fibrosis around the ulcer. The pancreatic juice was sterile, and the responses subsequently obtained suggested that functional impairment was slight in spite of the radiological appearances.

Methods.—

1. *Collection of Samples.*—Simple gravitational drainage without suction was used throughout. Repeated observations made in this way gave consistent results even during rapid changes in pancreatic activity.

2. *Estimation of Enzymes.*—Quantitative studies were confined to diastase, which was estimated by Wohlgemuth's (1908) method. The presence of tryptic activity was detected by digestion of fibrin on incubation for 24 hours at 37° C.

Observations on the Volume and Composition of Pancreatic Juice.—

1. *Total Volume.*—The daily output from the fistula is charted in *Table II*. The output of 2·4 litres on the first day of discharge suggests the release of accumulated

Table II.—Daily Output from Pancreatic Fistula

Post-operative Day	Output from Fistula	Post-operative Day	Output from Fistula
	millilitres		millilitres
1st	7	38th	1260
2nd	8	39th	1080
3rd	2400	40th	1320
4th	600	41st	1560
5th	720	42nd	1410
6th	1080	43rd	1740
7th	630	44th	1400
8th	617	45th	650
9th	810	46th	800
10th	960	47th	1100
11th	659	48th	450
12th	837	49th	660
13th	720	50th	420
14th	1020	51st	540
15th	420	52nd	760
16th	370	53rd	630
17th	123	54th	350
18th	90	55th	900
19th	75	56th	660
20th	100	57th	1020
21st	90	58th	900
22nd	240	59th	780
23rd	540	60th	840
24th	720	61st	800
25th	750	62nd	660
26th	340	63rd	630
27th	399	64th	540
28th	990	65th	300
29th	362	66th	960
30th	480	67th	630
31st	1212	68th	750
32nd	1600	69th	600
33rd	1640	70th	300
34th	1500	71st	270
35th	1202	72nd	120
36th	1350	73rd	60
37th	960	74th	—

fluid and has not been considered in calculating the average daily flow. The volumes from the sixteenth to the twenty-third post-operative days and for the last four days before closure of the fistula have been discounted because during these days marked tryptic activity was present in the jejunal juice. Over the remaining period of eight weeks the average daily output was 880 ml., but there were periods when the output was considerably over 1 litre for each consecutive day (*Table II*, post-operative days 31–44).

Over a period of eight weeks comparison of the patient's fluid intake with the output from the fistula showed no obvious correlation, but as no attempt was made to regulate the fluid intake, specific periods of high or low intake were not available for comparison.

2. *Twenty-four Hour Distribution.*—On six occasions hourly collections were made throughout the 24 hours. During each of these periods a Ryle's tube was passed until the tip was situated in the efferent jejunal loop just distal to the stoma (*Fig.* 310). In three of the six collection periods continuous jejunal aspiration was carried out between 9 p.m. and 6 a.m. In the remaining three only two samples of jejunal juice were aspirated during the night. In each of the six periods a pooled sample of jejunal aspirate was tested for tryptic activity. This was present in three of the six, indicative of an incomplete fistula, and the figures from these three observations have been discarded. In the remaining

three observations tryptic activity was not detected and the output from the fistula has been taken to represent the total external pancreatic secretion.

FIG. 310.—Radiograph showing position of Ryle's tube in the efferent limb of jejunum. Some lipiodol remains in the pancreatic acini and ducts, but barium has not passed back into the afferent jejunal loop.

The total enzyme output showed a direct relation to the volume of secretion.

The electrolyte composition of the pancreatic juice is shown in *Table IV*. The concentration of chloride was comparable to the plasma-chloride, whereas that of bicarbonate was considerably higher in the pancreatic juice. The concentrations of the two principal anions showed an inverse relationship (*Figs.* 312, 315). The potassium concentration in the pancreatic juice corresponded closely to that in the serum, but sodium

Table III.—MINIMAL HOURLY PANCREATIC SECRETION*

TOTAL OUTPUT IN 24 HR.	MINIMAL HOURLY VOLUME	CONTINUOUS ASPIRATION OF JEJUNUM
millilitres	millilitres	
800	12	Yes
1080	5	No
1020	4	Yes

* In each of these three experiments tryptic activity was absent from the jejunal aspirate.

maintained a concentration in the pancreatic juice significantly greater than in the serum (*Table V*). Both over the 24-hour period and over the shorter period covering the response to a meal, the two principal cations showed an inverse relationship to each other (*Figs.* 312, 313).

With serum concentrations of 5·1 to 5·3 mEq./l. the calcium concentration of the pancreatic juice varied from 2·9 to 3·03 mEq./l.

Response to Secretin and Pancreozymin.*—The intravenous injection of secretin resulted in a sharp increase in volume lasting from 15 to 30 min., depending

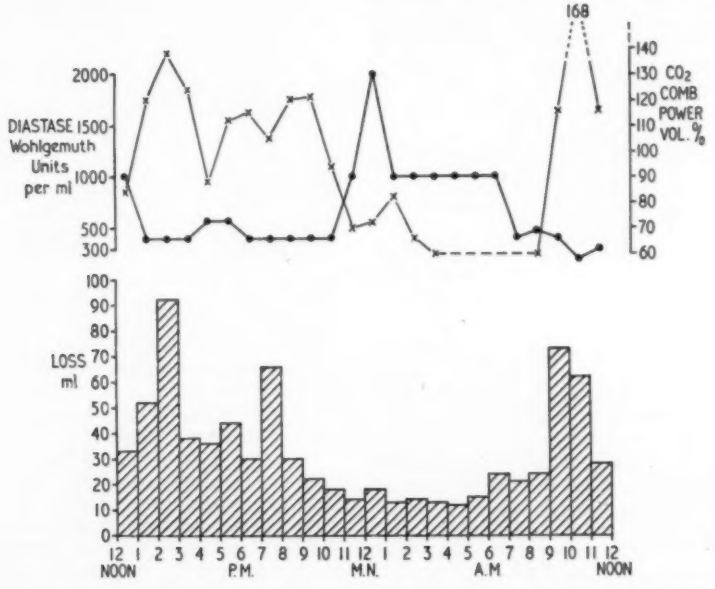

FIG. 311.—Pattern of pancreatic secretion over a 24-hour period, showing relation of alkalinity and enzyme concentration to volume.

The overall pattern of secretion was constant; copious secretion occurred in response to meals; the minimal hourly secretion was found during the early hours of the morning (*Fig.* 311). The minimal hourly secretion could not be related numerically to the total 24-hour volume or to the use of continuous jejunal aspiration (*Table III*).

3. *Composition.*—As was to be expected, a direct relation of alkalinity to volume, and an inverse relation of enzyme concentration to volume were found (*Fig.* 311).

on the dose (*Fig.* 314). The diastase concentration showed a slight rise during the first 15 minutes after the injection of secretin, but thereafter fell sharply to below

* The secretin and pancreozymin were supplied by Boot's Pure Drug Co. The limited quantities available permitted only the observations actually illustrated in the figures.

the previous level: the total output of diastase followed a similar curve except that the increase during the first 15 minutes was much greater owing to the increase in volume. The effect of secretin on bicarbonate output was a marked rise, but this took place more slowly than the volume response and was of much longer duration, so that the greatest bicarbonate concentration was reached

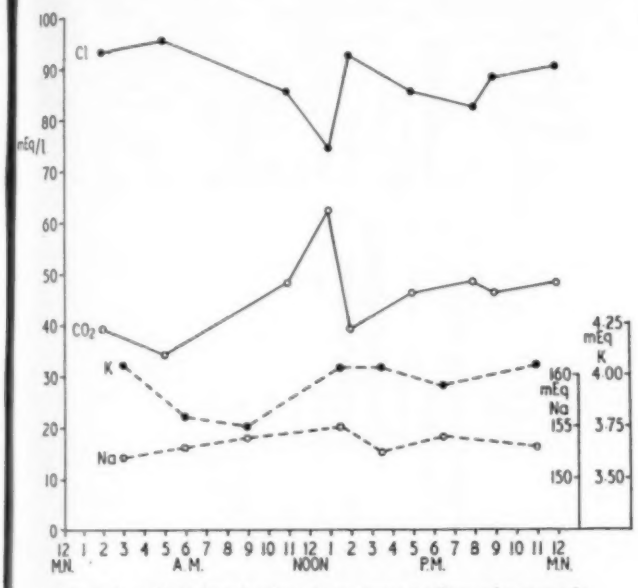

FIG. 312.—Variations in electrolyte concentrations of pancreatic juice over 24-hour period.

about 40 minutes after the maximal volume response at a time when this had returned to its previous level (*Fig.* 315). The changes in chloride concentration showed the usual inverse relationship to bicarbonate.

Table IV.—COMPOSITION OF PANCREATIC JUICE RELATED TO PLASMA VALUES IN THE SAME PATIENT

	PANCREATIC JUICE	PLASMA
pH	7·9–8·5	7·35–7·45
S.G.	1·004–1·010	1·025–1·030
Protein	0·1–0·2 g. per cent*	6·0–8·0 g. per cent
Chloride	63–95 mEq./l.	63·3–95·5 mEq./l.
Bicarbonate	27–87 mEq./l.	28·6–33·9 mEq./l.
Sodium	139–155·2 mEq./l.	131·7–141 mEq./l.†
Potassium	3·52–4·5 mEq./l.	3·23–4·86 mEq./l.†
Calcium	2·9–3·02 mEq./l.	5·2–5·3 mEq./l.†

* Only occasional pus cells present in centrifuged deposit.
† Serum concentration.

Table V.—CONCENTRATION OF SODIUM IN SERUM AND PANCREATIC JUICE

SERUM-SODIUM	PANCREATIC JUICE SODIUM
mEq./l.	mEq./l.
131·7	139–144·5
134·3	147·3
141·0	152–155·2

Intravenous injection of pancreozymin resulted in a much smaller but nevertheless definite increase in volume. The enzyme response was relatively no greater than with secretin and showed the same general characteristics (*Fig.* 314). The effect on bicarbonate and chloride was similar to, but much less than, the response following secretin (*Fig.* 315).

Effect of Drugs.*—

1. *Ephedrine*, 60 mg. intramuscularly, *atropine*, 0·6 mg. intramuscularly, *banthine*, 50 mg. intravenously, and *probanthine*, 30 mg. orally, were all effective inhibitors of pancreatic secretion (*Fig.* 316).

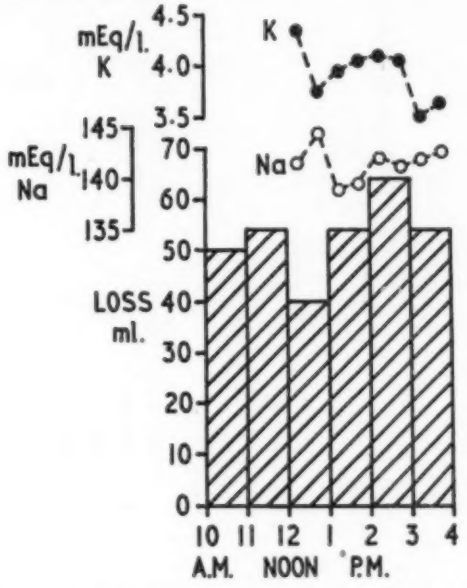

FIG. 313.—Relation between cation concentration of pancreatic juice and volume response to food.

2. The effect of *prostigmine* was extremely variable even when doses of 1·0 mg. intramuscularly were used. On the whole, a slight increase in volume seemed to result (*Fig.* 317), but there were several observations where this did not occur.

3. *Carbachol* by subcutaneous injection resulted in a modest increase in volume and a very great rise in diastase output (*Fig.* 318).

4. *Hydrochloric acid:* 10 ml. of *N*/10 acid were injected by Ryle's tube and washed through with 5 ml. of normal saline. The end of the tube was known to be lying in the jejunum just distal to the gastro-enterostomy stoma. An immediate increase in volume was observed which was proportionately greater than with any other stimulus. The total diastase output showed a sharp rise and fall corresponding to the volume of secretion (*Fig.* 319) and was associated with a slight increase in enzyme concentration.

5. *Alcohol*, given as brandy, 30 ml. by mouth (*Fig.* 320), *bile-salts* (Dehydrocholin, B.D.H., 1·0 g. by mouth) (*Fig.* 321), *soluble insulin*, 10 units intravenously (*Fig.* 325), and inhalation of *tobacco smoke* were all without detectable effect on volume output; enzyme estimations were not made.

Effect of Food.—The effects of carbohydrate, fat, and protein in isocaloric quantities were tested when these were given (*a*) by mouth, and (*b*) by tube directly into the jejunum. (The figures for the effect of jejunal instillation were based on only one observation in each case.)

The effects of carbohydrate and of protein hydrolysate were also tested by intravenous administration.

1. *Glucose*, 26 g. (107 calories) by mouth, produced a large and immediate increase in volume. The response

* Every observation in this and subsequent sections is based on at least two experiments, with the exception indicated below. Where the results were consistent, only one experiment is illustrated.

to *lactose* was equally great, but was spread over a slightly longer time. When glucose was injected directly into the jejunum, the volume response was comparable to that obtained after its oral administration (*Fig.* 322), but glucose, 25 g. (103 calories) given intravenously in 500 ml. change in volume on the other occasions when it was given by mouth or when given by jejunal tube (*Fig.* 323).

3. *Protein* was given as casilan in 30-g. doses (equivalent to 26 g. protein and 107 calories) and as hepamino in 32-g. doses (equivalent to 26 g. protein and

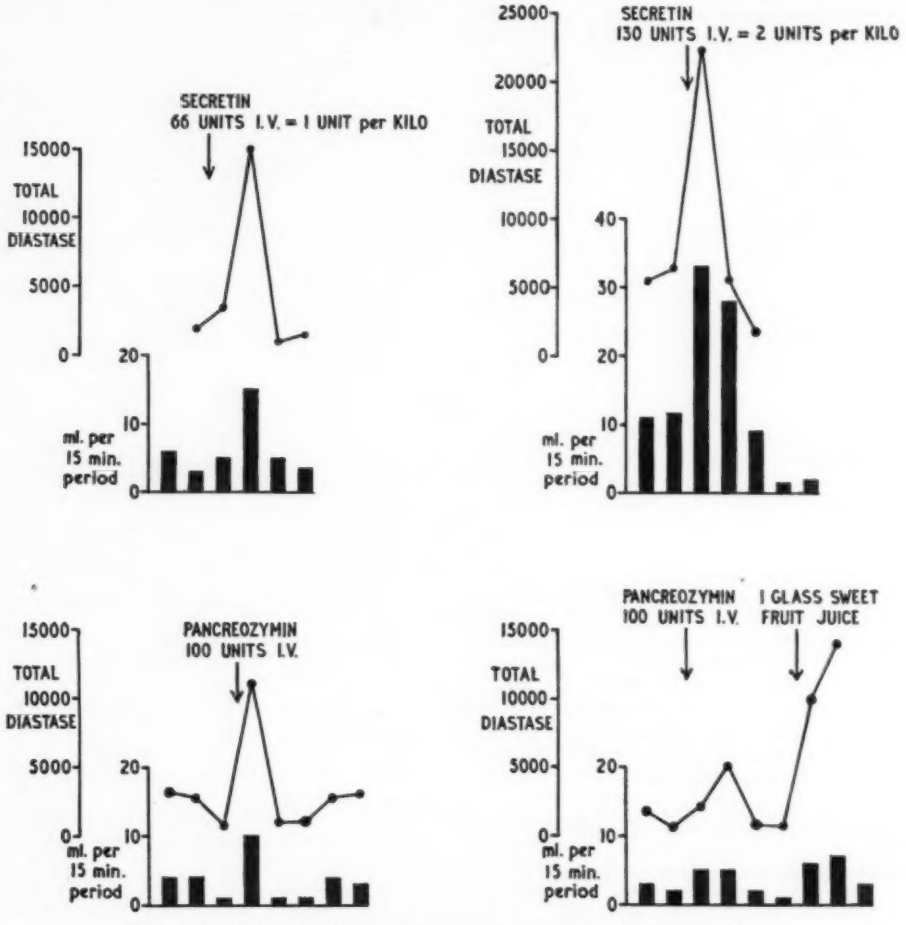

FIG. 314.—Volume and enzyme response to secretin and pancreozymin.

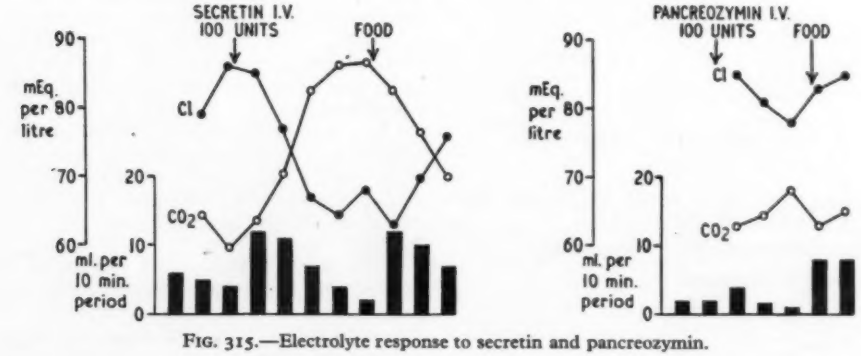

FIG. 315.—Electrolyte response to secretin and pancreozymin.

water, produced only a slight response in volume (*Figs.* 322, 325). The effect of carbohydrate on diastase output was a slight increase which was commensurate with the volumetric response. The concentration of diastase remained unchanged or fell slightly.

2. *Fat* was given as a fine emulsion of peanut oil containing 12 g. of oil in 30 ml. of emulsion (112 calories). In one test this emulsion appeared to produce a rise in volume and in total diastase output, but there was no

107 calories). The volume response was intermediate between those produced by fat and by carbohydrate. The response was slightly less than that obtained after the drinking of 150 ml. of milk* (*Fig.* 324). After jejunal instillation the volume response was comparable to that

* 150 ml. of milk supplied 106 calories as follows :— carbohydrate 30 calories, protein 20 calories, fat 56 calories.

obtained when protein was taken by mouth. The equivalent of 26 g. (107 calories) of protein was given intravenously as hydrolysate with 5 per cent glucose in

Excretion of Antibiotics.—Both aureomycin and terramycin were given intravenously over thirty minutes in doses of 500 mg. in 500 ml. of isotonic glucose or in

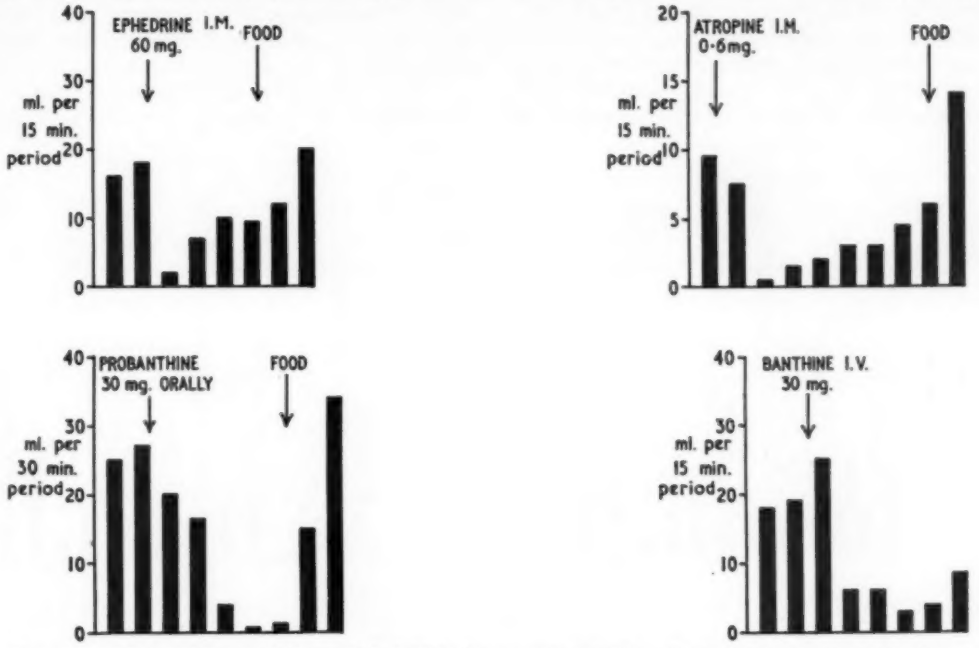

FIG. 316.—Effects of drugs which regularly inhibited pancreatic secretion. Note that in the case of atropine the time scale (abscissa) is half that used to illustrate the effects of the other drugs.

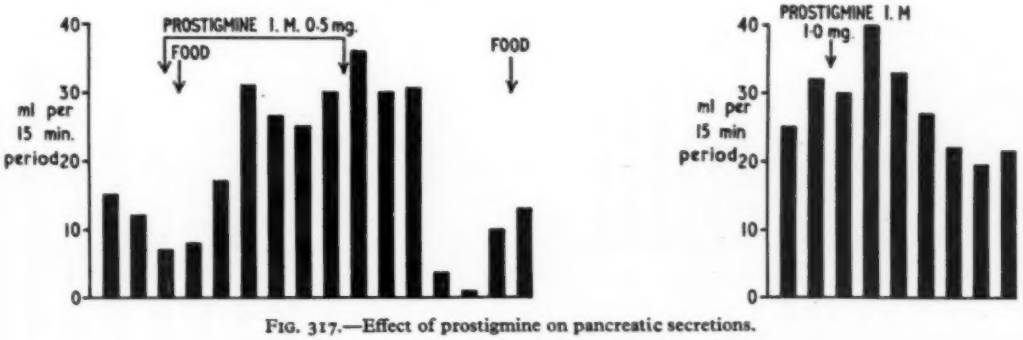

FIG. 317.—Effect of prostigmine on pancreatic secretions.

the form of casydrol, 520 ml. No increase in volume was observed (*Fig.* 325). The increase in total diastase output after ingestion of protein hydrolysate was accompanied by a slight but consistent increase in enzyme concentration.

Effect of Intravenous Fluid.—Normal saline, 600 ml. given intravenously over a period of 30 minutes and 1000 ml. given over 90 min., produced a slight transient increase in flow (*Fig.* 325). As already stated, only a slight change in volume was observed after infusion of 500 ml. of isotonic glucose and none after 520 ml. of casydrol in 30 min.

Sham Feeding.—When the patient was already very hungry, his lunch having been delayed during the completion of some observations, he was presented with an appetizing three-course meal. The main course was then removed and given to the patient in the next bed. The subject was instructed to start eating his soup, but, after savouring each spoonful, to spit it out without swallowing any. He carried this out faithfully, and no change in volume output from his fistula was observed. When an identical meal was put before him 45 min. later, a volume response was noted as soon as he began to swallow soup (*Fig.* 326).

600 ml. of normal saline. At no time during the following two hours was antibiotic activity detected in the pancreatic juice.

DISCUSSION

Volume and 24-hour Distribution.—The average daily output over eight weeks of study was 880 ml., but a much higher rate of secretion was maintained over periods of many days. The highest daily output of 1740 ml. is comparable to the output of 1770 ml. observed by Miller and Wiper (1944). On the day when 1740 ml. were collected, strong tryptic activity was detected in the jejunum so that the total pancreatic output was certainly greater than the measured loss. Miller and Wiper suggested that even their figure of 1770 ml. did not represent the total output because their patients' stools were normal, but they did not record daily output figures in relation to stool examinations and the loss of pancreatic juice might have been complete on the day cited without the presence of any gross abnormality in the stools. A 24-hr. pancreatic output of

over 1300 ml. has been recorded in several other cases of pancreatic fistula (Kahn and Klein, 1932, 1390 ml.; Snyder and Lium, 1936, 1384 ml.; Miller, Ginsberg, and Howard, 1950, 1342 ml.; Howard, James, and Evans, 1951, 1350 ml.) and Newman and Eisenstein (1949) reported an output which averaged 1250 ml. over several days. In cases of complete external fistula it has been suggested

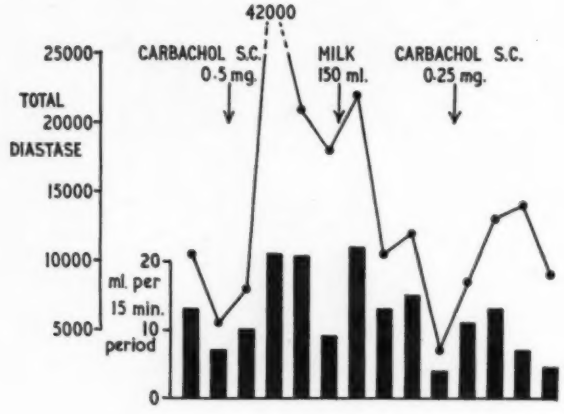

FIG. 318.—Effect of carbachol.

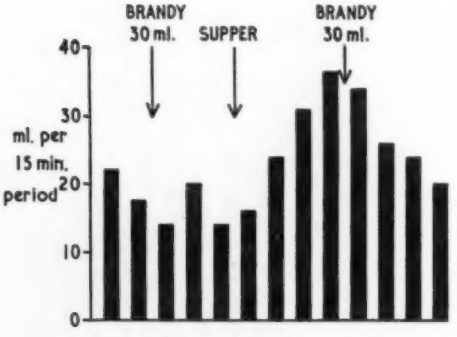

FIG. 320.—Effect of alcohol by mouth.

that the absence of pancreatic enzymes from the bowel removes an inhibitory mechanism and so results in excessive secretion by the pancreas. During the high output period shown in *Table II*, from the thirty-first to the forty-fourth post-operative days, the patient received 5 g. triple-strength pancreatin (Lilly) by mouth each day for the first week. Although enzyme replacement was not provided during the second week, there was no significant change in output. Therefore it seems unlikely that this level of secretion was due to loss of normal inhibitory control. The excellent response of the pancreas to the various stimuli employed makes it improbable that such high secretory rates were due to damage to pancreatic function as a result of the operative procedure. Moreover it is difficult to conceive of any mechanism whereby damage to the secretory cells could result in excessive secretion unless some specific reabsorptive activity were impaired and so far as is known such activity does not play a part in the normal process of pancreatic secretion. Controlled evidence of excessive secretion in pancreatic disease is absent except for one case in which diffuse carcinoma of the pancreas was associated with an excessive volume response to secretin (Lake, 1947). The absence of any obvious correlation between the state of hydration of the patient and the volume of pancreatic secretion is in keeping with the findings of Howard and others (1951).

Although in man pancreatic secretion is continuous throughout the 24 hours, it is doubtful whether it is

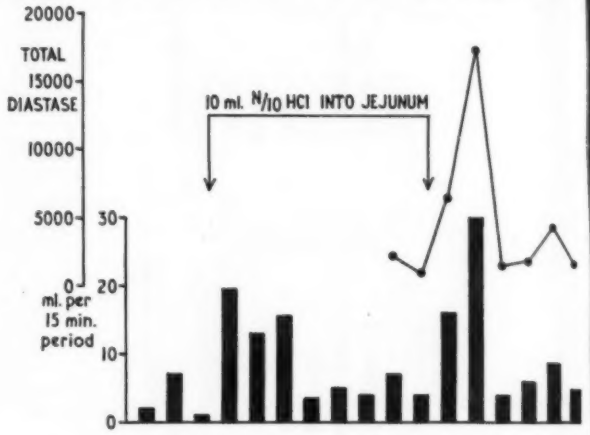

FIG. 319.—Effect of hydrochloric acid injected into the efferent loop of jejunum.

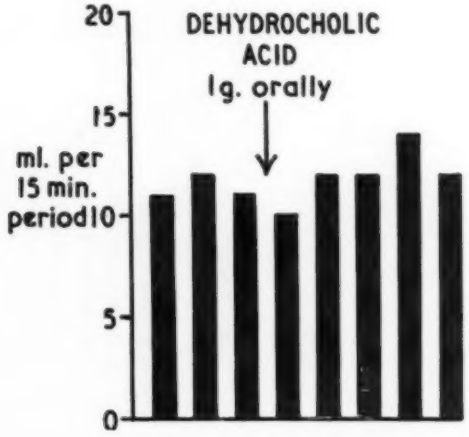

FIG. 321.—Effect of bile-salts by mouth.

truly spontaneous (Babkin, 1950). In the fasting subject, gastric juice and bile continue to enter the duodenum and the vagus remains active. Previous estimates of the fasting pancreatic secretion in man are given in *Table VI*. In none of these experiments was a prolonged period of fasting employed and the figures were based on only two to four 20-minute collecting periods. In Christiansen's (1933) and Voegtlin, Greengard, and Ivy's (1934) cases, precautions were not taken to prevent the entry of gastric contents into the duodenum. In the present case the duodenum was, of course, excluded from the gastric remnant and it was most unlikely that gastric contents would pass into the afferent jejunal loop when a thin barium emulsion could not be persuaded to do so (*Fig.* 310). The additional precaution of continuous aspiration of the efferent loop did not appear to reduce the volume of pancreatic secretion (*Table III*). From these considerations it seems

likely that the very low rate of fasting secretion recorded in the present case gives a better indication of pancreatic behaviour under basal conditions than do the earlier observations.

The vagal innervation of the pancreas in man reaches the gland through the cœliac and hepatic branches of the posterior vagal trunk (Hovelacque, 1927; Mitchell, 1953). In the present case the left gastric artery was ligated distal to the origin of the œsophageal branch and the tissues proximal to this point were not disturbed. Therefore it was improbable that the vagal innervation of the pancreas had been interrupted by the operative procedure. The role of vagal activity during sleep was not investigated by injection of atropine, but in view of the marked effect of atropine in reducing the volume of pancreatic juice during other tests, it seems likely that the vagus was responsible for at least part of the fasting secretion. Newman and Eisenstein (1949) found that atropine inhibited the flow of juice during the period of minimal secretion between 2 a.m. and 4 a.m., but this may have been secondary to inhibition of gastric secretion. Moreover, the action of atropine cannot be taken as absolute proof of vagal activity because the secretagogue effect of hyperglycæmia on the pancreas of some animals is abolished by atropine but unaffected by vagotomy (Hebb, 1935).

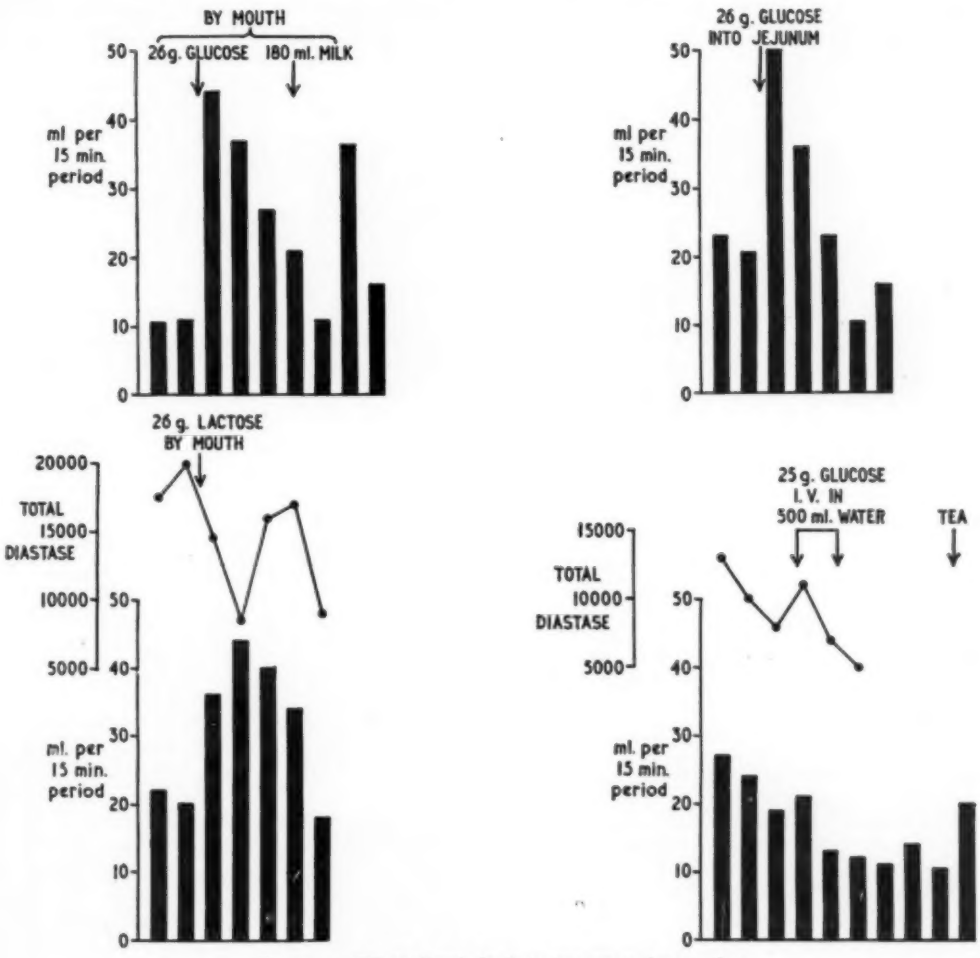

FIG. 322.—Effect of carbohydrate on pancreatic secretion.

Table VI.—PREVIOUS ESTIMATES OF FASTING PANCREATIC SECRETION IN MAN

MILLILITRES PER 60-MIN. PERIOD	AGREN AND LAGERLÖF	FRISK AND WELIN	CHRISTIANSEN*	VOEGTLIN,* GREENGARD, AND IVY
Maximum	99	99·0	195	222
Average	36	34·5	105	66
Minimum	0	3·9	12	30

* No precautions taken to prevent gastric juice entering the duodenum.

Note: The original experiments recorded volumes collected in 20- or 30-min. periods. These have been expressed as hourly volumes to facilitate comparison with *Table III*.

The part played by bile in the regulation of pancreatic secretion in man remains in doubt. Whereas Lagerlöf (1942) found some evidence that the presence of bile-salts in the duodenum stimulated the pancreas, McCaughan, Simmer, and Sullivan (1938) failed to confirm this. The negative results in McCaughan's case and in the present patient do not necessarily conflict with the observations of Lagerlöf, because in each of the cases giving negative

results a supplement of bile-salts was administered in the presence of a presumably adequate flow of bile, whereas Lagerlöf's observations were made on a subject in whom the normal flow of bile was eliminated. Another possible explanation for the failure in the present case to augment pancreatic secretion by bile-salts is that the dose administered was inadequate. On the basis of Fox's (1927)

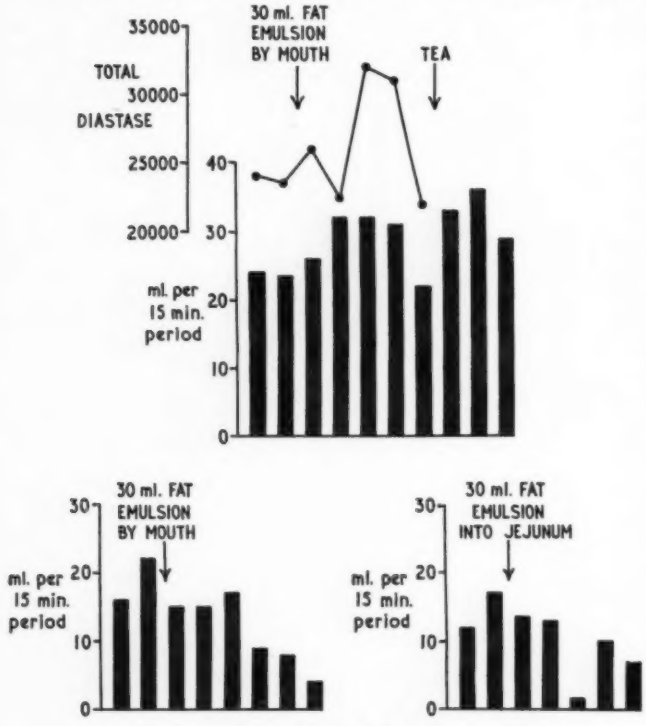

FIG. 323.—Effect of fat on pancreatic secretion.

estimate that gall-bladder bile contains an average of 6 per cent of bile-salts, a normally-functioning gall-bladder might be expected to contain, when full, about 3 g. of bile-salts. In each experiment only 1 g. of dehydrocholic acid was given as compared to 3 g. in Lagerlöf's study. In man, continuous or intermittent intestinal aspiration confirms that bile is almost invariably present in the duodenal content throughout the 24 hours, even in the presence of a normally functioning gall-bladder. It is thus theoretically possible that bile is a factor in maintaining the flow of pancreatic juice during fasting and sleep, but as the quantities entering the bowel during fasting are small even in comparison with the dose of bile-salts administered in the present tests, the part played by bile in the maintenance of fasting pancreatic secretion in man must be insignificant.

Electrolyte Concentration.—With the exception of the bicarbonate ion, it is generally stated that the concentrations of the principal electrolytes present in pancreatic juice correspond to their blood concentrations when these are expressed in the usual way as milliequivalents per litre of plasma. In this patient the sodium concentration in the pancreatic juice was repeatedly demonstrated to be significantly greater than that in the serum when so expressed (*Table V*). This difference has also been noted by Mahaffey and Haynes (1953) and appears in the figures published by Miller and Wiper (1944), who found that pancreatic juice contained 138 mEq./l. of sodium with a serum-sodium of 113·3 mEq./l. A possible explanation of this finding is the extremely low protein content of pancreatic juice. If the serum-sodium level is expressed as milliequivalents per litre of plasma water, the concentration of sodium is found to be about 9 mEq./l. higher than the figure as usually expressed, and the difference between the concentrations in serum and pancreatic juice becomes insignificant. The corresponding difference between potassium concentrations in serum and pancreatic juice would be much less obvious owing to the very small values involved and no such difference was found in the present case. However, the figures of Kogut, Matzur, and Sobel (1936) show a potassium concentration greater than the corresponding serum value by an amount which would fit in with this hypothesis; while Mahaffey and Haynes (1953) reported similar findings, although in their patient the difference between plasma and pancreatic juice was even greater. In the pancreatic juice of the dog, Ball (1930) made similar observations on sodium and potassium concentrations and suggested the same explanation. Such an explanation, however, does not adequately explain the observation in this patient of a reciprocal relationship between the concentrations of sodium and potassium ions in pancreatic juice. An inverse ratio between the concentration of chloride and bicarbonate has long been recognized and explained on the basis of a selective secretion of bicarbonate by the acinar cells, with secondary adjustments in chloride so as to maintain the total anion concentration at an approximately constant level. Such an explanation is less acceptable in the case of fixed base than in the case of bicarbonate, which may be, at least in part, synthesized by the acinar cells (Ball, Tucker, Solomon, and Vennesland, 1941). As pointed out by Davies and Ogston (1950) sodium may not be an ion which can undergo primary secretion, so that unless a suitable carrier is present to transfer sodium in an un-ionized form the secretion of sodium ions must be regarded as secondary to that of bicarbonate ions. The finding that in contrast with the bicarbonate concentration the sodium concentration in pancreatic juice varied inversely with the rate of flow is difficult to explain on any existing hypothesis of secretion. Further observations on the relationship between electrolyte concentration and volume flow are needed before definite conclusions can be drawn.

There has been considerable variation in the values given by different observers for the normal calcium content of pancreatic juice. The figures have in general been lower than those consistently obtained in the present case. On the assumption that about 60 per cent of the serum-calcium is present in diffusible form, a level of 3 mEq./l. is in the range which might be expected on theoretical grounds. The lower figures reported by some observers may have resulted from a technical error in the method of estimation. All calcium estimations on this patient were carried out by the method of Kramer and Tisdall (1923). In the first few determinations in which the samples were handled as for serum analysis, the results all lay between 0·75 and 2 mEq./l. It was noticed that the precipitate formed after addition of

ammonium oxalate had, when dried, a lack of cohesion such as characterizes the precipitate obtained from urine, in contrast to that from serum. The risk of loss of calcium during ashing was consequently much greater than in serum-calcium estimations. This source of error was overcome by the addition of a small amount of decalcified serum to the solution at the time of precipitation, as is done in urine calcium estimation. All subsequent results were over 2·7 mEq./l.

The protein content of pancreatic juice has been variously recorded as from 'a trace' up to 1 g. per 100 ml. In most reports no indication has been given as to the presence or absence of infection at the time of the estimation. It is obvious that the presence of pus cells will raise the protein content,

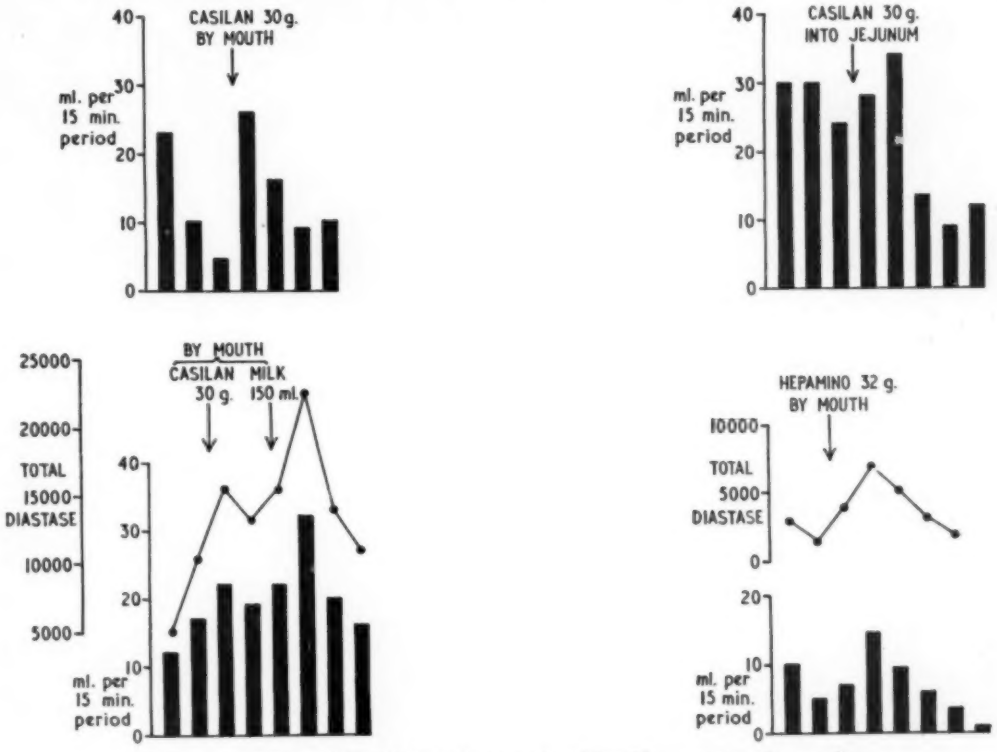

FIG. 324.—Effects of protein hydrolysate and amino-acids on pancreatic secretion.

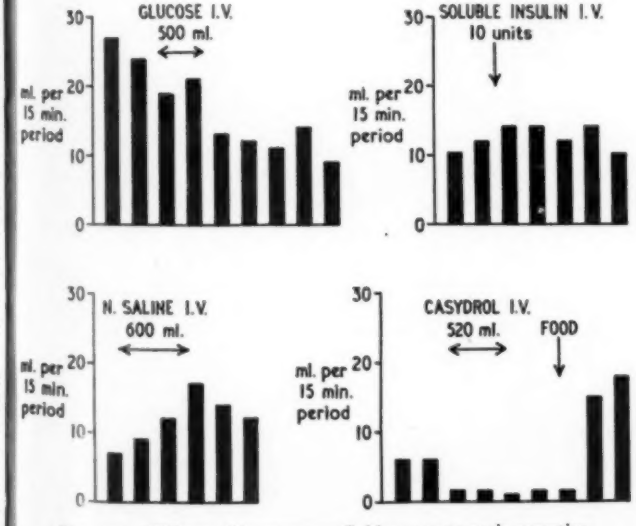

FIG. 325.—Effects of intravenous fluids on pancreatic secretion.

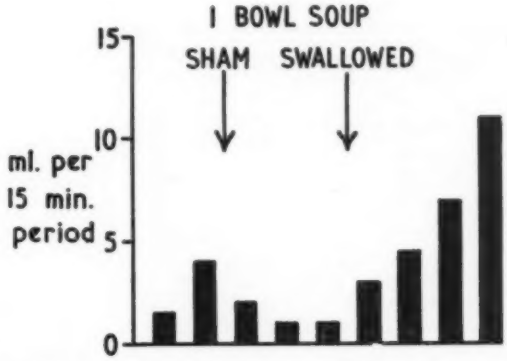

FIG. 326.—Effect of sham feeding to show absence of psychic response by the pancreas.

and the lowest figures reported are probably the most significant. The presence of inflammatory exudate may also explain the high figures for specific gravity sometimes reported (Lake, 1947; Howard and others, 1951), as the specific gravity is not necessarily a function of the rate of secretion (Snyder and Lium, 1936; Mahaffey and Haynes, 1953).

Effect of Secretin and Pancreozymin.—After the injection of secretin the pancreatic response conformed to the pattern already established in man by Lagerlöf (1942) and others, although the increase in volume was much less than that usually recorded by the method of duodenal aspiration. This

discrepancy cannot be explained by the absence of bile in the collected material because the bilirubin content of the duodenal content falls after administration of secretin (Diamond and Siegel, 1940; Lagerlöf, 1942), nor can it be accounted for by the absence of duodenal secretion from the samples because the volume response from a fistula has been shown to approximate closely to that obtained by duodenal aspiration (Lake, 1947). That the small volume might have resulted from impaired pancreatic function is not likely in view of the brisk increase in volume noted during other observations in the same subject. The low initial volume before injection of the enzymes suggests that at the time these observations were made the fistula may have been incomplete. Since tests for tryptic activity in the jejunum were unfortunately not made at the time, this cannot be proved, but it would appear to offer the most reasonable explanation of the response obtained.

The delay in bicarbonate response as compared to volume response has been noted previously in man by Agren and Lagerlöf (1936) and by Lagerlöf (1942) and is well illustrated in the figures published by Howat (1952) although he does not comment on this finding. Examination of the bicarbonate concentration in relation to the 24-hour volume distribution (*see Fig.* 311) reveals a similar tendency, the greatest bicarbonate concentration occurring in most cases during the hour following each volumetric peak. At this stage it is not possible to offer any explanation of this finding.

The response to pancreozymin was less satisfactory in that the enzyme output after injection was less than that produced by secretin. When related to the much smaller volumetric response after pancreozymin, the output of enzymes in each case was found to be comparable. The fact that the response to pancreozymin was qualitatively similar to that produced by secretin as regards volume, enzymes, and electrolytes suggests that the preparation used may not have been fully active or free from secretin. (The actual preparation was at that time in an experimental stage.) On the other hand, it is possible that the poor enzyme response to pancreozymin, and also the failure of carbohydrate, fat, and protein to stimulate enzyme production when tested individually, indicated a mild degree of impairment of pancreatic function. With slight functional impairment the production of enzymes, and especially of diastase, may be selectively affected while the volume response and production of bicarbonate remain unchanged (Agren, Lagerlöf, and Berglund, 1936; Diamond and Siegel, 1940; Lake, 1947).

Effect of Drugs and Foodstuffs.—The finding of Howard and others (1951) that alcohol markedly reduced the output from a pancreatic fistula has not been confirmed. An association between consumption of alcohol and attacks of pancreatitis is well recognized and has usually been attributed to obstruction of the pancreatic ducts by duodenitis and spasm of the sphincter of Oddi. The diminished volume of duodenal aspirate following alcohol ingestion has been explained in the same way. In this case, therefore, failure to influence the rate of pancreatic secretion by administration of alcohol by mouth was not unexpected.

In the case of drugs reinforcing or blocking the autonomic nervous system the results obtained in the present study conform in general to those of other observers. However, it was repeatedly found that atropine, ephedrine, and banthine were not effective in abolishing the response to food given during their period of action (cf. Snyder and Lium, 1936; Comfort and Priestley, 1943; Howard and others, 1951). The effects of prostigmine appear to be variable. McCaughan, Simmer, and Sullivan (1938) found a gradual increase in volume after a fifteen-minute latent period although the bicarbonate concentration fell. An increase in volume was also found by Snyder and Lium (1936) and by Howard and others (1951). Knight, Muether, and Sommer (1949) considered prostigmine to be so effective a stimulus as to justify its use in diagnostic tests of pancreatic function in man. An increase in secretion after physostigmine was reported by Miller and others (1950); on the other hand, Miller and Wiper (1944) reported a diminished volume after prostigmine and McCaughan and Purcell (1941) found a reduced volume after physostigmine. In the present case the results were equivocal although an isolated observation might have suggested either slight inhibition or slight stimulation of secretion. As suggested by Miller and Wiper, this variability may possibly be due to the fact that prostigmine acts on synapses in the sympathetic ganglia as well as on parasympathetic nerve-endings.

In contrast to the positive effect of carbachol, the absence of any definite effect following prostigmine might suggest that the vagal innervation of the pancreas had been damaged, but, as already indicated, this was not likely on anatomical grounds. It is known that in animals the efficacy of insulin-induced hypoglycæmia as a stimulus to pancreatic secretion depends on an intact vagal pathway (Babkin, 1950), but, as the response of the pancreas to hypoglycæmia is confined to the enzyme output with little or no increase in volume so long as gastric secretion is excluded from the duodenum and jejunum (Frisk and Welin, 1937), in this case the absence of any volume change after insulin is not significant as a measure of vagal activity.

In the intact subject hypoglycæmia produces a much greater effect on the production of gastric acid than on pancreatic enzymes and a copious secretion of alkaline pancreatic juice will follow the injection of insulin if gastric juice is available to initiate the secretin mechanism. That the pancreatic response to hydrochloric acid in this patient had not been materially affected by exclusion of the duodenum was shown in repeated tests. When the gastric juice was allowed to pass freely into the jejunum, the absence of any increase in flow of pancreatic juice after insulin injection was therefore evidence of complete removal or inhibition of the acid-producing gastric glands. This fact is germane to the interpretation of the results following the feeding of pure carbohydrate in the form of glucose by jejunal tube. Glucose by mouth has always been found to result in a definite increase in the volume of pancreatic secretion. In the intact subject this occurs after an initial delay of two to four hours, the longer delay being found especially when hypertonic solutions have been administered. This delay is presumably

due to the production of pylorospasm (Shay and Gershon-Cohen, 1934), an explanation which is supported by the fact that when the pyloric sphincter has been removed an immediate response to oral glucose is obtained (McCaughan and others, 1938; present case). In contrast to oral feeding, except in McCaughan's case glucose given by duodenal or jejunal tube has not previously been found to stimulate the flow of pancreatic juice. (From the wording of McCaughan's report there is some doubt whether the glucose was in fact injected directly into the jejunum.) It may be that in these two cases glucose introduced directly into the efferent jejunal loop passed back through the patent stoma to stimulate the production of acid by the gastric remnant, but the absence of any response to insulin when the gastric juice was allowed to pass freely into the jejunum and the persistent neutrality or alkalinity to litmus of the gastric aspirate in the present case suggest that this may not, after all, be the whole explanation. That the effect is not due to hyperglycæmia is shown by the very short lag period and by the failure of intravenous glucose to influence pancreatic output. Previous reports on the effects in man of various foodstuffs given by mouth are conflicting. Ellinger and Cohn (1905), Fast (1930), and McCaughan and Purcell (1941) reported that a high-fat diet gave the greatest and most prolonged volume response, but most workers have found that, as in this case, carbohydrate gives the greatest increase in volume of pancreatic juice and fat the least (Wohlgemuth, 1907; Graf, 1910; Holsti, 1913; Friedrich and Landislaus, 1922; Mocquot, Joltrain, and Laudat, 1933; Snyder and Lium, 1936; Comfort and Priestley, 1943; Comfort, Osterberg, and Priestley, 1943); so that the use of a low-carbohydrate, high-fat diet in cases of acute pancreatitis or of pancreatic fistula is probably rational.

The failure of intravenous glucose to increase enzyme secretion by the pancreas is in contrast to the experiments of Hebb (1935) in the cat and rabbit. The absence of any such effect in this case may have been due to inadequate stimulation because the blood-sugar was raised much more acutely in Hebb's experiments. The lack of evidence of any relationship between blood-sugar levels and disordered ecbolic function in cases of diabetes mellitus (Deusch and Drost, 1927; Agren and others, 1936; Pollard Miller, and Brewer, 1943) may likewise be due to inadequately high blood-sugar levels, but may on the other hand reflect a true species difference in pancreatic response. This seems the more likely because the effect of hypoglycæmia in many animals is to diminish the enzyme output from the pancreas (la Barre and Destrée, 1928; Baxter, 1932; Hebb, 1937), whereas in man an increased output is found (Okada, 1929; Frisk and Welin, 1937).

The volumetric response by the pancreas after intravenous infusion of isotonic glucose was no greater than that resulting from infusion of an equal volume of isotonic saline. This was also found by Miller and Wiper (1944), while Thomas and Ross (1948) reported no increase in the rate of flow from a fistula when 10 per cent glucose was injected intravenously. On the other hand, Howard and others (1951) found that 1 litre of 5 per cent glucose given intravenously in under one hour resulted in an increase of 50 per cent in the flow of pancreatic juice. Newman and Eisenstein (1949) also state that saline alone gave "slightly less response" than saline with 5 per cent or 10 per cent glucose. The resolution of this contradictory evidence would be of considerable practical importance in assessing the safety of intravenous glucose infusions in cases of acute pancreatitis. The infusion of protein hydrolysates was not found to increase pancreatic output, but the suggestion of Thomas and Ross (1948) that hydrolysates given intravenously inhibit pancreatic secretion was based on inadequate evidence from their own case and was not borne out by the present observations.

In contrast to what obtains in the stomach, there appears to be no true psychic secretion in the pancreas. Previous attempts to induce a psychic flow by Friedrich and Landislaus (1922), Villaret and Justin-Besançon (1925), and Kahn and Klein (1932) have all been as unsuccessful as the attempt in the present patient. The experiments of Newman and Eisenstein (1949), which purported to demonstrate a psychic phase in pancreatic secretion are invalid, as precautions were not taken to prevent access of gastric juice to the duodenum.

The failure of the broad-spectrum antibiotics to pass into the pancreatic juice has already been demonstrated by Howard, Pulaski, and Fusillo (1952) who rightly point out that this finding is irrelevant to the problem of antibiotic therapy in acute pancreatitis. On the other hand, in any attempt to prevent or control infection of the pancreatic ducts in the absence of acute inflammation (for example, in external pancreatic fistula), it follows that sulphonamides or penicillin remain the drugs of choice.

SUMMARY

Studies on the physiological responses of the pancreas have been made in a patient who developed an external pancreatic fistula after subtotal gastrectomy for duodenal ulcer.

The daily output of pancreatic juice is believed to be greater than has often been taught. Figures of the order of 1500 ml. are not considered pathological.

Previous findings relating to the 24-hour volume distribution have been confirmed.

Under basal conditions the rate of pancreatic secretion has been shown to fall to levels lower than those previously recorded in man. This slight secretion is considered to be mainly the result of continuing stimulation by the vagus and does not represent spontaneous secretion.

As conventionally expressed, the sodium concentration in the pancreatic juice is higher than that in the serum. Possible explanations for this have been discussed.

It is suggested that the low estimates of calcium concentration in the pancreatic juice given by some previous workers may be explained on the basis of a technical error in the method of estimation.

The reciprocal relationships between chloride and bicarbonate concentration have been confirmed and some evidence has been presented that a similar relationship exists between sodium and potassium ions.

Attention has been drawn to the dissociation between the volumetric and bicarbonate responses following stimulation of the pancreas.

In general the responses to various drugs have confirmed previous reports, but the effect of prostigmine is variable and in tests of pancreatic function this drug should not be used to stimulate secretion.

Various pure foodstuffs have been tested as stimulants of pancreatic secretion. It has been shown that carbohydrate is a much more powerful stimulant than either protein or fat. Administration of carbohydrate directly into the jejunum was found to result in a brisk flow of pancreatic juice. Possible explanations of this unexpected finding have been discussed.

Intravenous infusions of carbohydrate or protein hydrolysates were not found to stimulate pancreatic secretion.

The absence of a psychic phase of pancreatic secretion in man has been confirmed, as has the failure of the broad-spectrum antibiotics to reach the pancreatic juice.

I should like to express my thanks to Mr. K. Paterson Brown for his interest and encouragement during the conduct of these investigations.

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FRACTURES OF THE FOREARM TREATED BY OPEN REDUCTION AND PLATING

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THIS report is a review of fractures of the radius and ulna treated by open reduction and plating in the Orthopædic Department of the Western Infirmary, Glasgow, from January, 1948, to December, 1953, inclusive. The aim was to ascertain the final results in 54 forearm fractures.

INDICATIONS

The indications for open reduction in this series were :—

1. Fracture of the shafts of the radius and ulna in which satisfactory alinement and apposition of the fragments could not be obtained or maintained by manipulation and immobilization in a plaster cast.
2. Fracture of the distal half of the radius with dislocation of the inferior radio-ulnar joint.
3. Fracture of the shaft of the ulna with dislocation of the head of the radius (Monteggia).

METHOD OF TREATMENT

General anæsthesia and a pneumatic tourniquet were always used. The radius was exposed anteriorly between flexor carpi radialis and brachioradialis and the ulna by an incision along its subcutaneous border. The bone-ends were manipulated into position and the reduction maintained by four- or six-holed metal plates, the screws penetrating both cortices (*Fig.* 327). In the earlier cases a padded plaster from axilla to palm was applied and retained for about eight weeks, but in 37 later cases a pressure bandage only was applied and active movements of the wrist and elbow were allowed immediately after the operation.

FOLLOW-UP

Forty of the 54 patients were examined by the author and 7 by other surgeons. Six could not be traced and 1 had died. Good clinical records were available for the patients who were not seen. The shortest time between operation and follow-up was 2 years and 3 months, and the longest period 6 years and 10 months.

Thirty-nine cases were male and 13 female.

The age incidence is shown in *Table I.*

Table I.—AGE INCIDENCE

Age in years	10–20	21–30	31–40	41–50	51–60	61+
No. of Patients	16	11	10	7	7	3

The operative treatment was as follows :—

Fracture	*Bones plated*	
Radius and ulna	Radius and ulna	31
	Radius only	3
	Ulna only	3
Radius	Radius	14
Monteggia	Ulna	3
	Total	54

The patients were examined for range of movement in the affected elbow, wrist, and forearm as compared with the normal arm. In the 7 cases in which the follow-up was incomplete the range of movement at the last attendance was obtained from the records.

RESULTS

	Patients
Recovery of full movement	31
Restriction of movement	23

The 23 patients with defective movement were divided into 5 groups in which the only loss of movement was :—

	Patients
1. Loss of ½ pronation or less	5
2. Loss of ½ supination or less	3
3. Loss of less than ½ pronation and ½ supination	2
4. Slight loss of pronation and supination and loss of 20° wrist movement	6
5. Patients with a greater loss than any of the above	7
	23

The 7 patients in group 5 are described in more detail :—

Case 1.—A woman aged 54 fell on the arm and sustained a fracture of the upper third of the ulna with a comminuted fracture-dislocation of the head of the radius. The ulna was plated and the head of the radius excised. Two months later a mass of new bone was present anterior to the elbow-joint, causing almost complete loss of pronation and supination with a final range of flexion at the elbow of 135–75°.

Case 2.—Man aged 25. His arm was crushed under a tractor, causing a grossly comminuted fracture of the upper third of the ulna with subluxation of the head of the radius. The ulna was plated, but two years later was found to be un-united. Iliac chip grafting was performed. At the follow-up he had full movement in all joints apart from a two-thirds loss of pronation.

Case 3.—A man aged 54 was struck on the forearm by a lever and sustained a double fracture of the radius as well as a fracture of the mid-shaft of the ulna. The lower radial fracture was comminuted. The upper fracture of the radius and the fracture of the ulna were plated and an unsuccessful attempt was made to screw the lower radial fracture. Four years later he had loss of half supination, two-thirds pronation, and loss of 30° of wrist movement.

Case 4.—A man aged 44 suffered fractures of the humerus, radius, ulna, and carpus owing to his arm being caught in a machine. The fractures of radius and ulna were both compound and later required grafting. When last seen one year later he had half the normal range of movement in the elbow and wrist, with marked restriction of rotation.

Case 5.—A woman aged 43 had a deformity of the radius due to a previous fracture.

Case 6.—A woman aged 36 developed cross-union of the radius and ulna following an unsuccessful sliding

graft of the ulna. She had full elbow and wrist movement, but no pronation or supination.

Case 7.—A man aged 28 sustained a fracture of the radius and ulna and tibia and fibula in a motor-cycle

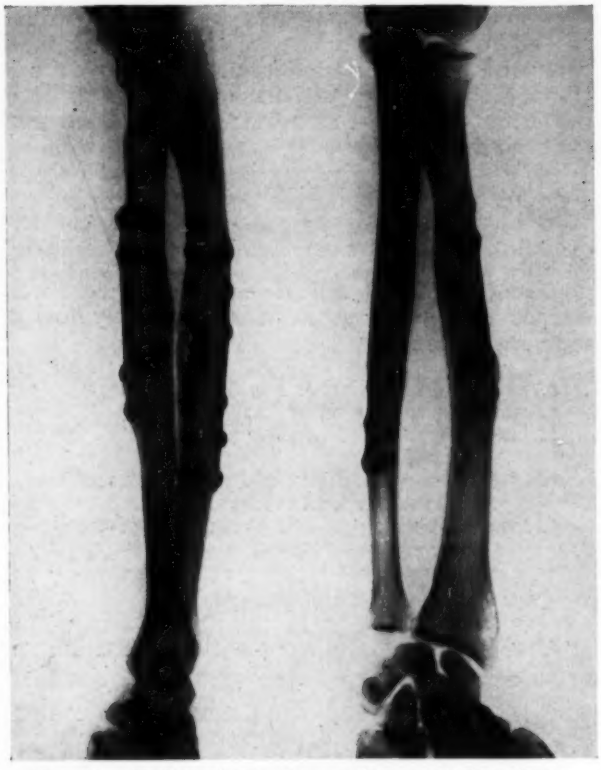

FIG. 327.—Radiograph of a forearm three years after plating of fractures of the radius and ulna.

accident. At operation marked œdema of the tissues of the forearm was noted. He later developed a slight flexion contracture of the long flexors of the digits and lost almost all supination.

Symptoms.—Thirty-six patients had no complaints; 12 had slight discomfort in the forearm when lifting very heavy weights; 7 patients were not interviewed.

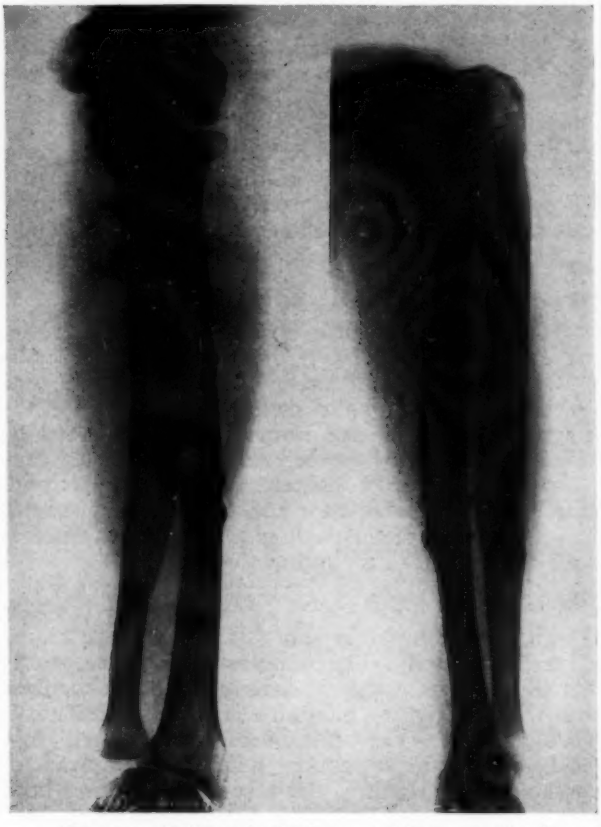

FIG. 328.—Radiograph of a forearm eighteen months after an onlay graft operation on the ulna for non-union following plating of the radius and ulna.

Deformity.—No patient had overt deformity of the forearm. In 10 the scar was broad, but none was keloidal.

Weakness of Grip.—This was complained of by only one patient, who suffered muscle damage at the time of the compound fracture.

Table II.—DETAILS OF PATIENTS REQUIRING BONE-GRAFTING

AGE	FRACTURE	COMPOUND SIMPLE	COMMINUTION	PLATING	GRAFT	METHOD OF GRAFTING	TIME AFTER FRACTURE
37	R. and U.	S.	U.	R. and U.	U.	Iliac chips	months 60
59	R. and U.	S.	—	R. and U.	U.	Iliac chips	5
34	R. and U.	S.	—	R. and U.	U.	Iliac graft	20
44	R. and U.	C.	R. and U.	U.	R. and U.	Tibial graft	3
36	R. and U.	C.	R.	R. and U.	U.	Slide graft	6
28	R. and U.	S.	U.	R. and U.	R. and U.	Iliac chips	5
39	R. and U.	S.	U.	R. and U.	R. and U.	Tibial graft	4½
46	R. and U.	C.	—	R. and U.	R. and U.	Iliac chips	3
19	R.	S.	R.	R.	R.	Iliac chips	3
25	U.	C.	U.	U.	U.	Iliac chips	24
50	R.	S.	R.	R.	—	—	—

Sepsis.—Sepsis did not occur, although 12 fractures were compound. Four patients had slight delay in healing of the skin wound.

Nerve Palsy.—Nerve palsy was present after operation in 7 patients. This affected the median nerve in 3 patients and the posterior interosseous in 4. The lesions were partial, of short duration, and recovery was complete. They were thought to be due to retractor or tourniquet pressure.

Time off Work.—Twenty-five patients with no other arm injury and who did not require grafting returned to work in about three months. Fourteen of these patients were working eight weeks after injury. The time off work of patients who required grafting but had no other injury was 4, 9, 5, 13, 11, and 4 months—an average of $7\frac{2}{3}$ months. In the remainder the time was affected by other factors.

Time of Bony Union.—Clinical and radiographic evidence of union was present at three months from the date of operation in 12 patients and at six months in a further 10. Accurate records as to the time were not available for the other 22 patients.

Delayed Union.—Ten patients required a bone-grafting operation for delayed or non-union. (*Fig.* 328.) One patient had no evidence of union seven months after operation, and as he has since gone abroad he has been regarded as a case of non-union. Thus the number of patients with delayed union or non-union was 11. Further details of these patients are given in *Table II.*

Possible Factors tending to delay in Union.—

Severe injury: Fifteen of the 54 patients had suffered severe injury, i.e., greater than a fall on the arm. Of these 15, 9 required grafting. The mode of injury of the patients with delayed union is shown in *Table III.*

Table III.—Mode of Injury in Patients with Delayed Union

Road accidents	4
Arm caught in machinery	3
Crush injury	3
Arm caught in swing	1
Total	11

Comminution of the fracture: Comminution was present in 8 of the 11 patients with delayed union, whereas only 2 of the fractures which healed without grafting were comminuted. The comminuted bone was not necessarily the one requiring grafting. (*See Table II.*)

Stability of internal fixation: In 7 of the 11 patients with delayed or non-union the surgeon found it difficult, or was unable, to obtain a completely stable reduction without a gap between the bone-ends.

External fixation: Seventeen patients had plaster applied after internal fixation, but in 8 patients this was necessary because of other injury or instability of the internal fixation. No comparison between the remaining 9 patients with external and internal fixation and the 37 patients with only internal fixation was attempted as there were other complicating factors.

Methods of grafting: In 6 patients the site of delayed union was exposed, the fibrous tissue excised with 'freshening' of the bone-ends, and cancellous bone from the ilium packed into the gap. The plate was removed only if it was loose. In 4 of these patients an arm plaster from axilla to metacarpal heads was applied, but in 2 patients it was not thought to be necessary. By this method union occurred in about ten weeks. Onlay tibial or iliac grafts were used in 3 cases and by this method union was slower. In the remaining patient a sliding ulnar graft was used and this was the only graft that failed. Cross-union occurred. The patient refused further operation as the forearm was comfortable in neutral pronation—supination with full function in the wrist and elbow.

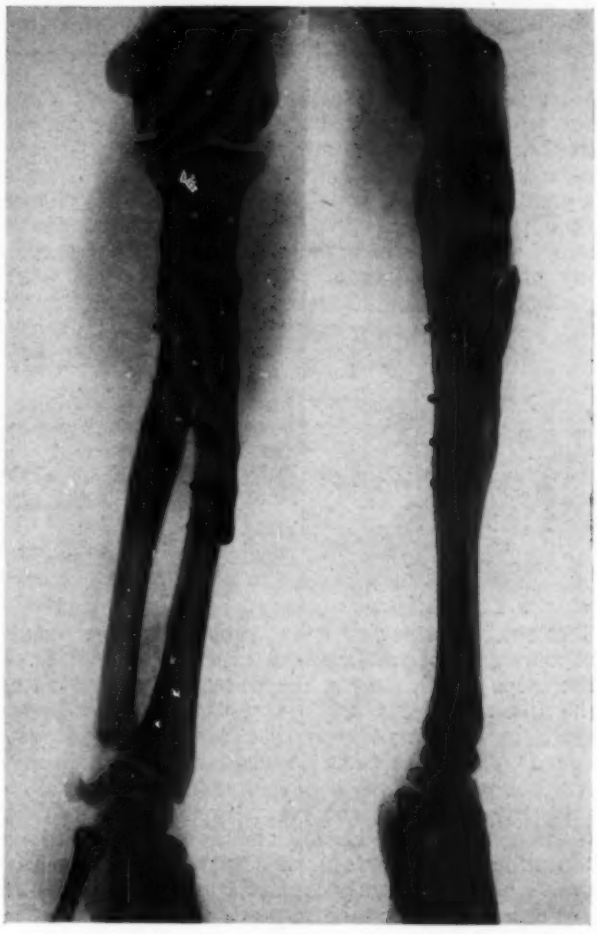

Fig. 329.—Radiograph showing non-union of a fracture of the ulna five years after plating of the radius and ulna.

Time of grafting: This varied with the individual surgeon. One surgeon operated if signs of union were not present at about four months whereas another would wait until there was established non-union.

The patient grafted five years after plating of the fracture was mentally defective and was found at the follow-up to have non-union of the ulna. Grafting was performed because he was having symptoms and the plate was becoming loose (*Fig.* 329).

A similar review of forearm fractures treated by plating was carried out in Sheffield by Holdsworth (1950). He reviewed 85 patients, of whom 75 were

men. No plaster fixation was used and grafting was necessary in only 4 patients. Sepsis occurred in 3 cases and 20 patients did not have a complete range of forearm rotation. (Holdsworth, 1950.)

CONCLUSION

Treatment of fractures of the shafts of the radius and ulna by open reduction and plating gives excellent results except where severe injury or comminution of the bones has occurred. In severe injury to the forearm there is, as would be expected, seldom a return to full function, but the final results from this method of treatment are usually better than after closed manipulation and plaster fixation. There is a greater incidence of delayed union in the comminuted fractures due either to damage to the blood-supply of the fragments or to the difficulty in obtaining a stable reduction. It may be politic when plating is required for the treatment of a comminuted fracture, or where good apposition of the fragments is not present in simple fractures, for the surgeon to surround the fracture site with cancellous bone-chips.

A post-operative plaster is seldom required for uncomplicated fractures and early return to light work is therefore possible.

Union of the fracture after plating is slow, but this is of litttle disadvantage to the patient unless it is slow enough to require grafting.

I am very grateful to Mr. Roland Barnes and to Mr. H. J. Seddon for their help in the preparation of this paper.

REFERENCE

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ANTERIOR SPINAL FUSION

A PRELIMINARY COMMUNICATION ON THE RADICAL TREATMENT OF POTT'S DISEASE AND POTT'S PARAPLEGIA

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THE object of this paper is to report the early results of a method of treatment of tuberculous disease of the spine which aims at the complete extirpation of the diseased focus and its replacement by bone-grafts in such a position that they are structurally sound. The authors do not claim that the method is entirely new. It is a development of ideas conceived by others in the past and made possible by advances in chemotherapy and anæsthesia, and by the adoption of architectural principles in arthrodesis—especially by the recognition of the initial and increasingly developing strength of a bony strut in compression.

A perusal of the literature dealing with the treatment of Pott's disease since the introduction of spinal fusion by Hibbs (1911) and Albee (1911) forty-five years ago shows that opinion on the value of posterior fusion is divided. Some advocate conservative treatment alone, some conservative treatment with late spinal fusion and others early spinal fusion followed by conservative treatment. There is no agreement on whether spinal fusion should be reserved for the adult or the child, or performed on both. This lack of unanimity suggests that there is no great advantage in posterior spinal fusion over conservative treatment. Henderson (1917) drew attention to the fact that posterior fusion does nothing to the diseased focus; to quote him: "neither the Hibbs nor the Albee type of operation for ankylosing the diseased area in tuberculosis of the spine is in any sense a radical operation for the extirpation of the focus of the disease"—an observation as true to-day as then. Girdlestone (1923) gave a lucid description of the spinal joints and emphasized that the Hibbs and Albee fusions are posterior spinal fusions and that they can only prevent flexion if the lateral columns of the spine are intact. King (1933) and McKee (1937) commented upon the fact that early spinal fusion can prevent collapse of the vertebral bodies anteriorly and so delay healing. Swett, Bennett, and Street (1940), in a pertinent appraisal of the pros and cons of spinal fusion, noted "the dominant role of the abscess in the healing process". Wilkinson (1955) advocates evacuation of the abscess and curettage of the lesion through a costotransversectomy. There is no doubt that throughout the world orthopædic surgeons are starting to be aware of the important part played by the abscess in delaying healing.

The spine was approached anteriorly by Muller (1906) before the introduction of the Hibbs and Albee operation. It would appear that the introduction of these two operations drew attention away from the lesion itself. Ito, Tsuchiya, and Asami (1934) published a series of 10 cases of spinal tuberculosis in which they approached the lumbar spine retroperitoneally in 8 cases, introducing an anterior graft in 2 cases and a second-stage Albee graft in 5 cases. One case of thoracic disease was approached through a costotransversectomy and bone-chips packed into the curetted cavity. This report was labelled a preliminary report and the follow-up of the earliest case was one year. We have been unable to find further reference in the literature to these cases. It is of interest to note that even in those pre-antibiotic days only two of the wounds broke down and we are told that they soon healed. Gjessing (1951) fused 2 cases of tuberculosis of the lumbar spine anteriorly.

We believe from a review of cases of recurrence of disease in our own series of posterior fusions that Swett and others (1940) and Wilkinson (1955) are

right when they emphasize that healing in this disease does not take place in the presence of an abscess. This is especially true in the thoracic region, where the abscess is enclosed and subject to the motions of respiration and to the beat of the heart and pulsations of the aorta. We agree with Seddon (1935) when he states: "There is a strong case for every effort being made to reduce the bone destruction during the active stage of caries of the thoracic spine."

The literature on the pathology of tuberculosis of the spine is sparse when one considers the frequency of the disease. Willis (1926) drew attention to the existence of extensive lesions of the spine which only superficially erode the bone. Cleveland and Bosworth (1942) have drawn attention to the "constant recurring states of sclerosis and caseation" and have shown the sclerosis to be due to aseptic necrosis. Wherever the primary site of the lesion, it travels by subligamentous spread which strips the ligaments from the vertebral body. When the ligaments are detached the blood-supply is lost and aseptic necrosis ensues. Fraser (1914) states that healthy bone has great resistance to tuberculous infection and this has been seen in our cases where healthy bleeding bone is seen close to a tuberculous focus. The bone with yellow marrow which Fraser postulated was devitalized by an exotoxin produced by the tubercle bacillus is really bone which has undergone aseptic necrosis. It would appear that the subligamentous spread with resultant aseptic necrosis is the important reason for the spread in the thoracic region, and in this fact may lie part of the reason for the better prognosis in the lumbar region where the abscess gravitates down the psoas sheath. In children the periosteum and ligaments strip easily and consequently lumbar as well as thoracic lesions are liable to be extensive. The positive stripping characteristic of this abscess had led us to name it a *dissecting paravertebral abscess*. These observations have been made during the anterior approach to our cases and are best seen in the thoracic region where the abscess finds difficulty in escaping and where it is subject to the action of the heart, aorta, and lungs.

While it would appear unlikely that systemic antibiotics could penetrate an abscess (Mackenzie, 1954), we have had many abscesses which have been proved sterile to the usual culture methods and to guinea-pig inoculation. The very bulk of the abscess, however, forms a mechanical barrier to anything but slow healing.

THE AIMS OF THE METHOD

It appears to us that decompression of the abscess with removal of the pus, caseous material, granulation tissue, intervertebral disks, and sequestra is imperative to arrest further vertebral destruction where the disease is progressing, in much the same way as is early decompression of an acute osteomyelitis to prevent chronic osteomyelitis with sequestration. Unless the spine is approached anteriorly the extent of the disease must remain unknown by present clinical methods, for we have found almost invariably that the gross lesion is more extensive than the radiographs suggest. It is possible to leave a clean, raw bleeding cavity when this stage has been completed and it remains to make the spine stable. We have felt that the obvious place to fuse the spine would be anteriorly where there is the largest portion of bone and where the graft would be in compression and with adequate protection (Brittain, 1942). It should hypertrophy according to Wolff's law and

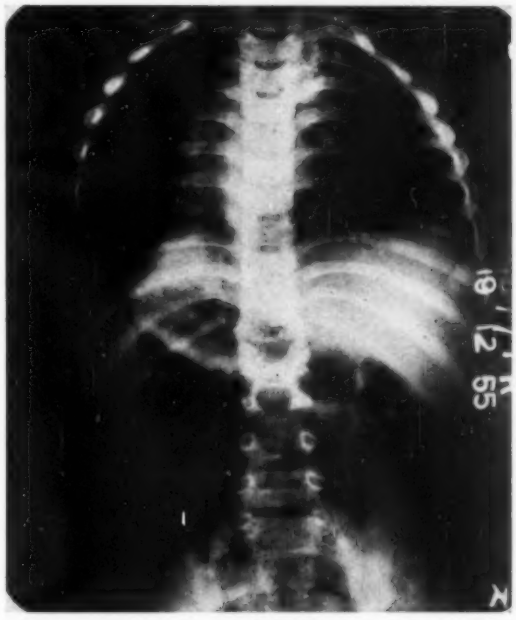

FIG. 330.—Large paravertebral abscess which has become shut off from the healing spinal lesion by fibrosis but has penetrated the lower lobe of right lung.

fulfil Percival Pott's criterion of healing, that fusion of the bodies of the vertebræ "was the thing aimed at". This is Nature's way of healing the disease, but it takes a long time and only occurs in about one in four patients (Cleveland, 1940). It is noteworthy that tuberculosis of the spine is the only tuberculous disease which does fuse spontaneously. We were dissatisfied with the exposure afforded by costotransversectomy as we found the operation difficult and the field restricted. Through this approach it was impossible to determine the extent of the lesion or to evacuate it completely, neither could the graft be inserted with any accuracy.

When we commenced this study we were unaware of the article by Ito and others or their earlier references.

OPERATIVE TECHNIQUE

Approach.—The approach to the spine anteriorly presents few difficulties and differs little from the approach to other structures in the vicinity.

The cervical spine is adequately reached by an incision along the anterior border of sternomastoid reflecting that muscle backwards, and the œsophagus, trachea, larynx, and carotid sheath forwards. If an abscess were present and pointing posteriorly the incision could be made along the posterior border of sternomastoid, but this has not yet occurred in our series.

The cervicothoracic region is one of the most inaccessible levels, but may be approached by a periscapular incision similar to that used for a first-stage thoracoplasty. The scapula is lifted with a mechanical retractor such as Edwards' and the third rib is

resected. The pleura is opened, but, if necessary, or if the pleura were very adherent, an extra pleural approach could be made easily at this level as in Semb's apicolysis. Access is limited, but the region from C.6 to D.4 is reached without undue difficulty. The superior intercostal artery should be divided at its origin together with the accompanying vein.

The approach to these two levels may be made on either side with equal ease and the choice is determined by the site and size of the abscess, being made on the side of the larger abscess. Below the level of D.4, however, in both thoracic and lumbar regions, we have found it much more satisfactory to approach the spine from the left side where the pulsating aorta provides an easily identifiable landmark in what may be a mass of fibrous tissue and abscess. An exception is made to this rule if radiologically the abscess appears to be penetrating the right lung, or if on account of its chronicity the abscess may be dissociated from a spinal lesion which is partly healed and replaced by much hard fibrous tissue (*Fig.* 330, *Case* 24). An abscess of almost any size can be evacuated from either side provided the diseased spine is adequately resected. It is only in the exceptional patient that we have approached the spine on the right side where the vena cava may be very difficult to identify and particularly exposed to damage.

In the thoracic region from D.4 to D.12 the thoracotomy should be performed by rib resection so that the rib is available for the graft. It is much easier to work downwards than upwards on the spine and the rib to be resected should always be above the level of the spinal lesion. The correct rib may be selected from the anteroposterior film of the chest by counting the ribs at the extreme lateral margin of the film and taking the one which at that point is level with the upper border of the lesion. Thus, a lesion of D.8 to D.10 will probably be most easily approached through the 7th or 6th rib.

The dorsolumbar spine is another difficult region and neither the thoracic nor lumbar incision is adequate. We have, however, made use of Fey's 11th rib incision which was devised as an approach to the upper pole of the kidney and the suprarenal gland. Through this incision good access is obtained from T.11 to L.5, but, if the disease extends higher, the 10th rib may be resected and the diaphragm separated posteriorly so that the peritoneum may be displaced forwards. If the disease does not extend above L.1 the 12th rib approach to the kidney described by Digby (1941) and others gives good access, while, if the upper limit of disease is L.3, the incision need not extend backwards beyond the tip of the 12th rib. Through this incision a large presacral abscess may be evacuated by suction and swabbing without difficulty.

In order to approach the spine with ease and safety, it is desirable to enter the abscess cavity as early as possible. In the thoracic region it is covered by pleura and intercostal vessels, and we therefore mobilize the aorta by dividing the pleura lateral to it, and ligating and dividing the intercostal arteries close to their origin together with tributaries of the hemiazygos vein. A vertical incision is then made into the wall of the abscess close to the midline and medial to the distally placed ligatures. At the upper and lower ends of this incision which extends to the visible edge of the abscess, transverse extensions are made so that a flap consisting of abscess wall, intercostal vessels, and pleura may be lifted and hinged laterally. This gives better access than

FIG. 331.—Graft in position. Two complete bodies have been removed and a strut placed anteriorly. The posterior cavity has been filled with match grafts.

FIG. 332.—Grafts in position. Two strut grafts have been placed in position and the space between them filled with match grafts. Only the anterior graft is firmly impacted.

either a single transverse or cruciate incision which we used in early cases. These incisions are made and the flap is lifted by diathermy needle dissection because the tissue is very vascular and the minute vessels are more readily coagulated than secured by forceps. This flap is held back by a suture.

In the lumbar region the lateral aspect of the spine is covered by psoas muscle and this must be either reflected or divided before the spine is reached. In the region of T.12 to L.1 the upper margins of psoas may be reflected downwards, but if the disease

FIG. 333.—'Calcification' in abscess cavity. The small opaque shadows are sequestra and the lower body shows ischæmic necrosis.

does not extend above L.3–4 a simple transverse incision through that muscle may be made with a diathermy needle, bearing in mind the trunks of the lumbar plexus which lie on its deep surface.

Evacuation of the Diseased Focus.—As soon as the abscess is opened, pus is evacuated and some material saved for culture, inoculation, and histological examination. All diseased tissues, pus, sequestra, aseptic necrotic bone, and devitalized disks are removed. The pus can best be removed by a sucker, while the rest are removed with a combination of osteotomes and a variety of nibblers. It is important to make sure that the full extent of the disease has been removed as it is easy to leave some disease behind. It is also important to remove the whole of the diseased vertebræ as far back as the spinal cord, as there is usually a posterior intraspinal abscess (Swett and others, 1940). When this toilet has been completed, a clean bleeding cavity should remain.

Insertion of the Graft.—It is possible to correct the kyphosis partially by direct pressure on the spine posteriorly. A mortise is made in the vertebræ at either end, the distance measured with dividers, and a strut graft of the correct length introduced to keep the vertebræ sprung apart. The interval which remains between the vertebræ is filled with small match grafts. We usually fashion the strut graft from rib which has been removed during the approach, while the match grafts are made from frozen banked bone. In the cervical and lumbar regions, however, both strut and match grafts have been made from banked bone (*Figs.* 331, 332). The flap of pleura and fibrous tissue is sewn back loosely.

Post-operative Treatment.—This presents no serious problem. The patient is placed in a plaster

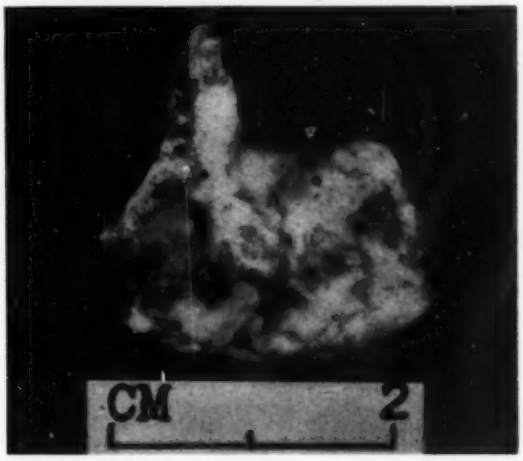

FIG. 334.—A sloughed intervertebral disk removed from the abscess cavity.

bed previously prepared with an anterior shell and is nursed for a considerable time prone.

Chemotherapy commenced pre-operatively is continued in the post-operative period.

When the chest has been opened, we have not usually found it necessary to use an underwater seal drain, but have relied on intermittent aspiration of fluid or air. Frequently no aspiration has been required.

The patient is allowed up as soon as there is clinical evidence of fusion.

RESULTS

Fourteen of the first 17 patients in this series have fused rapidly and soundly despite the fact that the time interval is relatively short. In the remaining 31 cases fusion is incomplete although many are showing encouraging evidence of fusion.

Fusion has been assessed both radiologically and by clinical methods. The spine becomes clinically stable about eight to twelve weeks after the operation as judged by the 'spring' and 'stethoscope' tests. The spring test consists of 'springing' the area of disease with the patient lying prone when there is a definite sense of give when the spine is unstable. The stethoscope test depends on the transmission of a true note across the fused area where the stethoscope is placed at one end of the fused area and the other end is percussed with the fingers.

The results of treatment are shown in tabular form in *Table I.*

COMPLICATIONS

1. Acute Dilatation of the Stomach.—This has occurred in 2 patients with disease of the lumbar

spine and has responded to treatment by gastric suction.

2. Hæmothorax and Pneumothorax.—This has occurred in several of the thoracic cases but has never been persistent. In all cases it has responded to aspiration, and the chest film has been completely clear within two weeks.

FIG. 335.—Large bilateral paravertebral abscesses which were completely evacuated from the left side after removal of the diseased bodies.

FIG. 337.—The swollen ballooned-out body below the main diseased area is a shell containing pus.

3. Convulsions.—Two patients with cervico-dorsal lesions have developed severe convulsions approximately twelve hours after the operation and lasting for twelve to twenty-nine hours. Both patients recovered. There seems to be little doubt that these resulted from sensitivity to streptomycin which had been placed within the evacuated abscess cavity and thus in direct contact with the theca. We have now discontinued the practice of dusting the cavity with streptomycin and merely use the drug systemically.

FIG. 336.—Small dense vertebral bodies which might suggest healing but are in fact ischæmic and necrotic.

4. Death.—There has been 1 death in the series. This child of 9 years, with extensive disease from D.12 to L.5 inclusive, had been under conservative treatment for six years and had been treated by posterior fusion without success. He was extremely ill but stood up to an extensive resection of six vertebræ very well. He became pyrexial on the third day and deteriorated rapidly and died. The cause of death was bronchopneumonia, probably aggravated by over-administration of intravenous saline.

DISCUSSION

While it is far too soon to pretend to estimate long-term results, we feel satisfied that the procedure is a great advance in treatment by cutting the duration of treatment from years to months and in preventing gross vertebral destruction with the resulting deformity. The anterior approach has unveiled the pathology of the disease in the living, which has not been universally appreciated, and this has led to a better understanding of the disease process. Some of these features are :

1. The Abscess.—The character of the pus is an indication of the activity of the lesion—thin, fluid, greenish pus denoting activity and thick, white pus chronicity. These observations have corresponded with the results of the tuberculin test. It is impossible to aspirate the pus completely. Harris

and Coulthard (1940) found abscesses in 90 per cent of their patients. We would go further and say that every case has an abscess unless it is very early disease or it has healed. We do not feel that calcification in the pus denotes healing; sometimes this 'calcification' is in sequestra and only indicates that the case is of some duration (*Fig.* 333). In the lumbar region the abscess may track down the front of the sacrum into the pelvis.

2. Disks.—While we were aware that disks were resistant to tuberculous infection, we were surprised to find that whole disks could remain at the site of the lesion as sloughs (*Fig.* 334). There is no doubt that they form a bar to bony ankylosis and in some cases can produce pressure on the spinal cord.

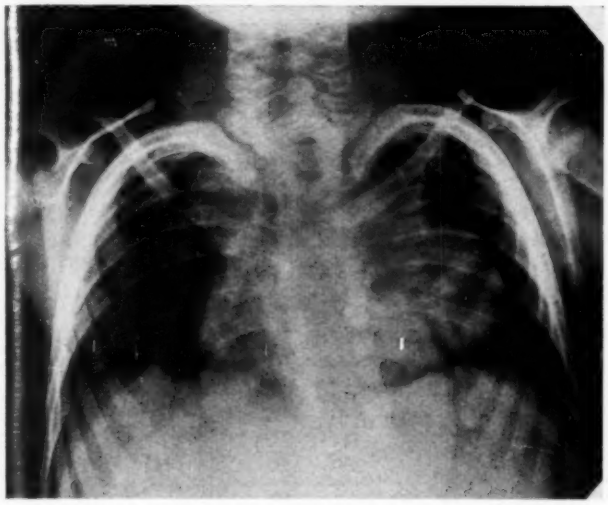

FIG. 338.—A rapidly enlarging paravertebral abscess which has penetrated the apex of the left lower lobe of lung.

3. Radiographs.—The long narrow shadow which has been considered to be a paravertebral abscess may be due to thickening of the tissues covering the spine, periosteum, ligaments, and pleura and may reach the thickness of 1 in. A more bulbous paravertebral shadow indicates pus (*Fig.* 335). Debris and calcification and ischæmic necrosis can give a dense shadow which gives a false impression of early healing (*Fig.* 336). Sometimes sequestra are difficult to pick up radiologically, but on re-examination of the pictures after the operation they can often be seen. Vertebral bodies whose outlines change from concave to convex and become slightly enlarged are affected by the disease and may be simply a bony shell containing pus (*Fig.* 337).

4. Penetration of the Lung by the Abscess.—While we were aware that cases had been described where the aorta had been perforated by an abscess (Simpson and Grabbilaar, 1955) and that the abscess could rupture into the pleura, it has not occurred to us that the lung was likely to be involved. In 6 of our cases the lung has been involved and has demanded treatment of the lung as a separate step in the operation (*Figs.* 330, 338).

In these cases it has been possible to curette out the lesion in the lung which has been surrounded by a thin zone of atelectasis. The cavity has been dusted with streptomycin and closed by suture. Resection has not been necessary. This small group of patients is being made the subject of a separate communication.

5. Correction of the Kyphosis.—It has been found possible to correct the kyphosis to a greater or lesser extent, greater in active disease and less in chronic disease with fibrosis. In a well-healed lesion the fibrosis is extremely tough and has to be cut with an osteotome at times, and although there are no radiological signs of ossification it appears to be pre-osseous.

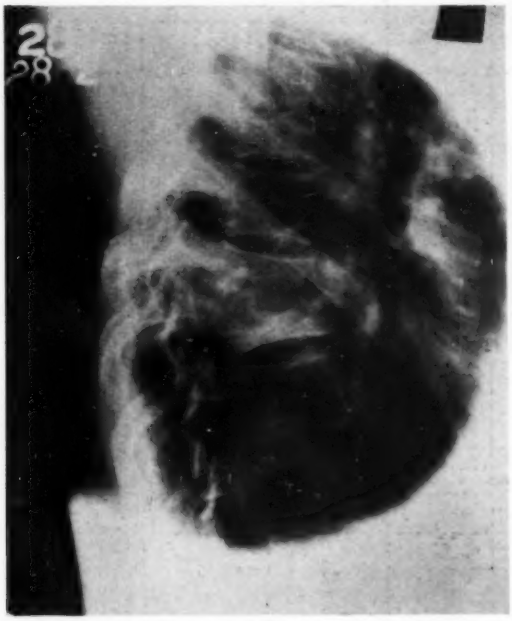

FIG. 339.—Vertebral collapse with retropulsion of both sequestrum and intervertebral disk causing paraplegia.

6. Paraplegia.—"It is high time that fresh light should be thrown on the treatment of Pott's paraplegia" (Girdlestone, 1949).

In the early cases we noticed how easy it would be to decompress the spinal cord from the front. We found no difficulty in this when we operated upon our first patient with complete paraplegia (*Case* 13). We found that the cord was pressed on by retropulsion of the vertebral body into the spinal canal (*Fig.* 339). The decompression was performed with ease, all the retropulsed vertebra was removed and we could see that it had been evacuated completely. Fixation of the spine was done at the same time by the introduction of an anterior graft, care being taken to protect the cord from the graft. The second case was a much more advanced case with involvement of D.8–D.11 (*Case* 18) and all these vertebral bodies had to be removed. The cord was eventually decompressed from D.8 to D.11. The whole cord had been stretched around these vertebræ, but the main pressure was at the apex of the kyphosis where there was a definite groove in the cord. In cases of recent paraplegia the recovery of the paralysis is dramatic, taking only a few days. The longer the duration of the paralysis, the longer the recovery takes and the less complete it is.

We have been surprised by the very high incidence of a posterior intraspinal abscess in patients

Table I.—C

No.	Name	Age	Sex	Duration	Level	Paraplegia	Previous Treatment	Abscess	
								Clinical Evidence	Operative Finding
1	T. Y. C.	22	F.	6 yr.	L.2, 3, 4	None	Aspiration of abscess. Posterior fusion, 8.7.52. Antibiotics	Present	Present
2	C. S. K.	6	F.	1 yr.	D.8, 9, 10	None	Plaster-of-Paris bed and antibiotics 6 mth.	None	Present
3	C. L. F.	8	F.	1 yr.	D.8, 9, 10	None	Plaster-of-Paris bed and antibiotics 6 mth.	Present	Present
4	H. S. W.	8	M.	2 yr.	D.8, 9, 10	None	Plaster-of-Paris bed and antibiotics 18 mth.	None	None
5	W. C. K.	5	M.	3½ yr.	D.11, 12; L.1, 2, 3	None	Plaster-of-Paris bed and antibiotics 6 mth.	Present	Present
6	C. H. L.	9	F.	2 yr., 2 mth.	D.8, 9, 10	None	Plaster-of-Paris bed and antibiotics 21 mth.	None	None
7	L. S. L.	9	F.	6 yr.	D.8, 9, 10, 11, 12	Developed June, 1954	Plaster-of-Paris bed and antibiotics 5 yr. Posterior fusion, 5.1.54	Present	Present
8	H. K. C.	7	F.	4 yr.	D.11–L.4	None	Aspiration of abscess. Plaster-of-Paris bed and antibiotics 14 mth.	Present	None
9	K. L.	6	F.			Weakness	Plaster-of-Paris bed and antibiotics 11 mth.	Present	Present
10	S. K.	6	M.	2 yr.	D.10–L.1	None	Plaster-of-Paris bed and antibiotics 6 mth.	Present	Present
11	L. A. N.	3½	F.	6 mth.	D.10, 11	None	None	None	Present
12	M. T.	21	F.	4 yr.	D.11, 12; L.1, 2	None	Plaster-of-Paris bed and antibiotics 3 yr.	Present	Present
13	C. W. K.	40	M.	1 mth.	D.7, 8	Rapidly developing and complete paraplegia	None	Present	None
14	K. K. H.	18	F.	2 yr.	D.5, 6	None	Plaster-of-Paris bed. Posterior fusion, 28.12.54. Antibiotics 1½ yr.	Present	Present
15	C. K. H.	4	M.	1 yr.	D.6–9	None	Plaster-of-Paris bed and antibiotics 4 mth.	Present	Present
16	W. S. C.	4	F.	1 yr.	L.3, 4	None	None	None	With vertebral bodies
17	C. T. Y.	3½	F.	3 mth.	C.4–6	None	None	Present	Present
18	P. C. Y.	33	M.	11 yr.	D.8–11	Paraplegia for 4 wk.	Plaster-of-Paris bed. Knee fusion, 1952	None	Present
19	L. Y. M.	3½	F.	1 yr.	*a.* L.3, 4 *b.* D.4–11	Weakness of lower limb	Posterior fusion of L.3–4. Plaster-of-Paris bed and antibiotics prior to first fusion	Present	Present
20	H. S. H.	21	F.	3 yr.	L.1, 2	None	Plaster-of-Paris bed 8 mth.	None	Small intravertebral
21	T. M. K.	3	F.	1 yr.	D.11–L.2	None	Plaster-of-Paris bed and antibiotics 4 mth.	Present	Present
22	L. F. T.	27	M.	6 yr.	D.10, 11, 12	Present	Posterior fusion, November, 1953. Antibiotics 4½ mth.	None	Present
23	Y. W.	37	M.	1 yr.	D.7, 8, 9	Two months complete with incontinence	None	Present	Present
24	M. K.	9	F.	7 yr.	D.6–12	None	Plaster-of-Paris bed and antibiotics off and on 7 yr.	Present	Present
25	L. M. C.	4½	F.	1 mth.	D.8, 9	None	None	None	Present
26	M. L. C.	3½	M.	2½ mth.	*a.* D.2, 3 *b.* L.1, 2 *c.* L.4, 5	None	Plaster-of-Paris bed and antibiotics 6 mth.	None	Present
27	C. K.	34	F.	9 yr.	L.4, 5	None	Posterior fusion, 1953	None	Present
28	C. H. S.	7	F.	1 yr.	D.9, 10	None	Plaster-of-Paris bed and antibiotics 11 mth.	None	Present
29	T. S. Y.	7	F.	6 mth.	L.2, 3	None	None	None	Present

CLINICAL HISTORIES OF 48 PATIENTS

Operative Findings	Operation Date	Fusion: Clinical	Fusion: X-ray	Remarks	Bacteriology
Present	1 .55	Satisfactory	Satisfactory	Persistent abscess and sequestra at operation	Negative smear, culture, and guinea-pig
Present	5.1 .55	Satisfactory	Satisfactory	Abscess invading lung—chronic caseous abscess and sequestrum	Negative smear, culture, and guinea-pig
Present	9.1 .55	Satisfactory	Satisfactory	Abscess evacuated	Negative smear, culture, and guinea-pig
None	9.1 .55	Satisfactory	Satisfactory	This child had a healed but unstable spine	
Present	11.1 .55	Satisfactory	Satisfactory	The strut graft fractured without displacement and was surrounded by callus. Collapsed somewhat four months later	Negative smear, culture, and guinea-pig
None	16.1 .55	Satisfactory	Satisfactory	A healed but unstable spine with many pleural adhesions	
Present	19. .55	No spring; stethoscope good	Satisfactory	There is a residual abscess D.12. This body should have been removed. Clinically well. ? result in one year	Negative smear, culture, and guinea-pig
None	23.1.56	Incomplete, 30.4.56	Fusing	Presacral abscess. Subsequently evacuated	Negative culture and guinea-pig
Present	30.1.56	Satisfactory	Satisfactory	Weakness of both limbs. Necrotic material in vertebral cavity	
Present	17.1.56	Satisfactory	Satisfactory	Abscess invading lung	Histology: tuberculous granulation tissue
Present	29.1.56	Satisfactory	Satisfactory	Minimum pus and abscess	Negative smear, culture, and guinea-pig
Present	4.1.56	No spring; fair note	No	Technical failure as L.1 and L.2 disk not removed. Complication—acute dilatation of stomach	Negative smear and culture. Guinea-pig died at 3 wk.—test inconclusive
None	11.1.56	Satisfactory	No	The paraplegia cleared within a few days of operation. Walking 28.4.56	
Present	31.1.56	Satisfactory	Satisfactory	Adhesions between abscess and lung. Movement present in spite of intact posterior graft and where movement occurred disease was present	Positive culture and guinea-pig
Present	9. .56	Satisfactory	Satisfactory	Slightly spastic	Negative smear, culture, and guinea-pig
With vertebral bodies	9.2.56	Satisfactory	Satisfactory	An early stage disease ideally suitable for treatment	Negative smear, culture, and guinea-pig
Present	16.2.56	Satisfactory	Satisfactory	Gone home in plaster collar	Negative smear, culture, and guinea-pig
Present	21.2.56	No spring; poor note	Too early to assess	Paraplegia recovered quickly. Adhesions in pleura. Grafted 6–12	
Present	.2.56 4.3.56	Too early to assess	Too early to assess	*a*. Involved lung. Sequestra. Post-operative convulsions *b*. Two sequestra, granulation tissue, and pus. (Pre-operative clonus much less.)	Negative smear, culture, and guinea-pig. Histology: tuberculous granulation tissue
Small intra-vertebral	7.2.56	? Spring; note fair	Too early to assess	L.1 and L.2 were brittle owing to aseptic necrosis. Slight superficial wound infection	Negative smear, culture, and guinea-pig. Histology: tuberculous granulation tissue
Present	1.3.56	Satisfactory	Satisfactory	Sequestra—much pus—graft towards right	
Present	6.3.56	Satisfactory	Fusing	D.12 large sequestra—posterior abscess pressing on cord. Paraplegia almost gone on 28.4.56	Positive smear, culture, and guinea-pig. Histology: tuberculous granulation tissue
Present	8.3.56	No spring; stethoscope note	Too early to assess	Finger prolongation of abscess along ribs 7–10	Histology: tuberculous granulation tissue
Present	3.56	—	—	Abscess in thorax involving lung—no abscess in spine—healed and fused by fibrous tissue anteriorly	Negative smear, culture, and guinea-pig
Present	5.3.56	Too early to assess	Too early to assess	Very early case—D.8 and D.9 avascular necrosis	Negative smear, culture, and guinea-pig
Present	.56 6. .56	Too early to assess	Too early to assess	*a*. Involving lung. Sequestra—pus. Superficial wound infection and breakdown due to avitaminosis *b*. L.1 and L.2 lesion more healed than in D.2–3 *c*. Not yet explored	Negative smear, culture, and guinea-pig
Present	3.56	Too early to assess	Satisfactory	Abscess, disk, and sequestrum at operation	Histology: tuberculous granulation tissue
Present	9.3.56	Too early to assess	Satisfactory	Early case	Negative smear, culture, and guinea-pig
Present	9.3 6	Too early	Too early	Avascular necrosis L.2 and L.3	Negative smear, culture, and guinea-pig

Table I.—CLINICAL HISTORY

No.	Name	Age	Sex	Duration	Level	Paraplegia	Previous Treatment	Abscess	
								Clinical Evidence	Operative Finding
30	H. M. C.	46	M.	3 yr.	D.6, 7	9 mth.	Costotransversectomy, 6.9.55	Present	Present
31	C. M.	38	F.	6 yr.	L.3, 4, 5	None	Posterior fusion, 1953. Plaster-of-Paris bed	Present	Present
32	W. S. L.	4	M.	16 mth.	L.1, 2	None	Plaster-of-Paris bed and antibiotics 3 mth.	None	Abscess in bone
33	S. K.	26	M.	6 mth.	L.1, 2	None	Antibiotics 3 mth. for pulmonary lesion	Present	Present
34	S. C. Y.	10	F.	6 yr.	L.3, 4, 5	None	Antibiotics	None	None
35	N. O. K.	5	M.	1 yr.	D.9, 10	None	Antibiotics 4 mth.	None	Present
36	C. H. Y.	3½	F.	2½ mth.	D.6, 7	None	Plaster-of-Paris bed and antibiotics 2 wk.	None	Present
37	A. W. C.	29	F.	3 yr.	L.2, 3	None	Plaster-of-Paris jacket. Antibiotics 3 yr.	None	None
38	W. T. S.	6	M.	3 yr., 4 mth.	D.7–D.10	Present	Laminectomy, 25.9.54. Posterior fusion, 21.3.55	None	Present
39	N. M.	5	F.	10 mth.	D.7–11	9 mth.	Antibiotics 10 mth.	None	Present
40	L. A. M.	5	M.	1½ yr.	D.8–11	None	Plaster-of-Paris bed and antibiotics 10 mth.	Present	Present
41	T. W. K.	13	M.	7 yr.	D.4–S.1	None	Plaster-of-Paris bed	Large abscess	Large abscess
42	P. M. C.	9	M.	6 yr.	D.12–L.5	None	Posterior fusion, 16.11.54. Plaster-of-Paris bed and antibiotics 5 yr.	Present	Present
43	L. L. O.	3½	F.	11 mth.	L.3–S.1	None	Plaster-of-Paris bed and antibiotics 6 mth.	None	Present
44	C. H. P.	3	M.	1½ yr.	D.11–L.3	None	Plaster-of-Paris bed and antibiotics	None	None
45	W. P. O.	2	M.	1 yr.	D.2–6	None	Plaster-of-Paris bed and antibiotics 1 yr.	Ruptured into left pleural cavity	None
46	L. T.	45	M.	4 mth.	L.3, 4	None	Antibiotics	None	Present
47	P. M. M.	7	M.	3 yr.	D.8–L.2	Impaired walking	Plaster-of-Paris bed and antibiotics 1 mth.	None	Present
48	Y. S. K.	5	M.	1½ yr.	D.4–10	6 mth.	Antibiotics 1 yr.	None	Present

without paraplegia. These patients are on the verge of disaster and this hidden danger is an added indication for the anterior approach to the spine and full decompression of the spinal canal in all patients.

CONCLUSION

The anterior approach to the spinal column is a practicable proposition at all levels. It is the only approach which allows accurate visual assessment of the extent of the disease. It offers the prospect of early radical treatment of Pott's disease and the prevention of paraplegia by the evacuation of the abscess from within the spinal canal. It allows complete evacuation of the abscess and decompression of the spinal cord in established paraplegia. It allows a bone-graft to be placed in the position where it is most likely to succeed. Because of the complete eradication of the disease it offers the hope of shortening the period of hospitalization.

It opens the study of the condition to detailed investigation in the future.

SUMMARY

1. The literature on the pathology and treatment of Pott's disease of the spine is reviewed.

2. A radical method of treatment consisting of complete extirpation of the disease and fixation by bone-graft in compression is described in detail.

3. The early results of treatment in 48 patients are tabulated and complications enumerated.

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48 PATIENTS – *continued*

OPERATION DATE	FUSION		REMARKS	BACTERIOLOGY
	Clinical	X-ray		
3.4.56	Too early to assess	Too early to assess	Sclerotic vertebræ. Paraplegia caused by body pressure and angulation. Some lessening of spasticity after operation. Note: (1) Presacral abscess; (2) Destructed vertebral bodies filled with pus	
[illegible].56	Too early to assess	Too early to assess	Active disease—necrotic vertebræ—femoral nerve in psoas partly divided—anæsthesia. Femoral—quadriceps palsy	
[illegible]4.56	Too early to assess	Too early to assess	D.12 removed by error. Early case ideally suitable for treatment. Graft to left of midline	Negative smear, culture, and guinea-pig
[illegible]4.56	Too early to assess	Too early to assess	1300 c.c. pus—active L.1 and L.2. Avascular necrosis	Positive smear and culture. Histology: tuberculous granulation tissue
[illegible].56	Too early to assess	Too early to assess	Sclerotic bone	
12.4.56	Too early to assess	Too early to assess	Abscess bulging into pleural cavity	Direct smear negative; culture positive, good growth
12.4.56	Too early to assess	Too early to assess	Abscess extending into apex of lower lobe; 240 c.c. fluid aspirated from pleural cavity 4 days after operation	Direct smear negative, culture positive
17.4.56	Too early to assess	Too early to assess	Lesion fairly well healed	
19.4.56	Too early to assess	Too early to assess	Frank pus adjoining dura. One month later clonus gone. Plantar reflex flexor	Histology: tuberculous osteomyelitis
26.4.56	Too early to assess	Too early to assess	Big abscess stretching across involved vertebræ	
27.4.56	Too early to assess	Too early to assess	Posterior abscess within spinal canal	
27.4.56	Too early to assess	Too early to assess	Drainage of tuberculous abscess only	
1.5.56	Too early to assess	Too early to assess	Extensive disease. Poor condition. Died third day of bronchopneumonia	
3.5.56	Too early to assess	Too early to assess	Pus, sequestra, and sloughed disks	Histology: tuberculous granulation tissue
3.5.56	Too early to assess	Too early to assess	Very little pus, lesion healing	
4.5.56	Too early to assess	Too early to assess	Lesion stable and healed at operation. Convulsions 12 hr. after operation lasting 29 hr.	
8.5.56	Too early to assess	Too early to assess	L.2 avascular and necrotic	
10.5.56	Too early to assess	Too early to assess	Two vertebræ were found to be hollow shells with pus. L.3 slightly distended but not explored. ? involvement	Histology: tuberculous granulation tissue
11.5.56	Too early to assess	Too early to assess	Immediate and progressive improvement of partial paraplegia	

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LESIONS OF THE ILEUM ASSOCIATED WITH ULCERATIVE COLITIS*

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THERE have been considerable differences of opinion regarding the clinical significance and incidence of lesions of the lower ileum in cases of ulcerative colitis. For while it is generally agreed that the most commonly found type of ileitis is caused by a retrograde spread from the diseased colon, and the term 'backwash' has been used, this mechanism does not explain all cases. There is another type of ileitis which is occasionally found proximal to a partially obstructed ileostomy. This condition, originally recognized and called 'ileostomy dysfunction' by Warren and McKittrick (1951), is characterized pathologically in the more severe cases by the presence of ulcers in the ileum which superficially resemble those of the retrograde type of ileitis. It is suggested that as a result of this resemblance, these two conditions have in the past been confused and considered as variants of the same pathological process. The resultant failure to differentiate the one from the other has led to the gravest consequences.

With regard to the rare cases of regional ileitis (Crohn's disease) associated with ulcerative colitis, although usually readily distinguished on gross pathological grounds from the types of ileitis already mentioned, they must be considered in any study of the pathology of the ileum in ulcerative colitis.

Finally there is the condition described by Brooke and Cooke (1951) of 'ileocolitis'. It has been suggested that this is primarily an ileojejunitis associated with steatorrhœa which produces secondary changes in the colon indistinguishable from those of ulcerative colitis.

It is proposed to review the literature, and present and analyse cases of the various types of ileal disease found in association with ulcerative colitis which have been observed at St. Mark's Hospital during the last three years, in the hope that this will help to clarify the clinical significance and pathology of this difficult and confused subject.

RETROGRADE ILEITIS IN ULCERATIVE COLITIS

The extension of an inflammatory process into the terminal ileum in patients suffering from ulcerative colitis, although fairly well recognized, has not been sufficiently emphasized. For some time it was thought that the ileocæcal valve would limit the spread of ulcerative colitis proximally, in the same way as it had originally appeared to limit the distal extension of terminal ileitis (Crohn, Ginsburg, and Oppenheimer, 1932), but it is now recognized in certain cases of both conditions to act merely as a temporary barrier.

Review of the Literature.—The first reference to ileal involvement in ulcerative colitis appears to have been made by Hale-White in 1888, after studying the pathology of 11 post-mortem specimens, in some of which an associated ulceration of the small intestine was observed. Although the term 'ulcerative colitis' was a "Guy's invention", to quote Woodward (1881), and originated in the lectures on Pathological Anatomy given by Wilks and Moxon published in 1875, several earlier pathological descriptions of 'dysentery', which undoubtedly included ulcerative colitis, were given by Rokitansky (1849) and Virchow (1853). Rokitansky noted not only that the disease "not infrequently passes beyond the cæcal valve towards the ileum", but also that the ileal pathology was usually less severe than that in the colon. At an earlier date Sydenham (1669–72) gave accurate clinical descriptions of "the bloody flux or dysentery". Allchin and Pitt in 1885 separately exhibited cases of ulcerative colitis to the Pathological Society of London, the former specifically mentioning that the ileum was normal. There were several notable papers on ulcerative colitis in the early part of the twentieth century, including those by Hawkins (1909), who described the natural history of the disease in 85 cases, J. Y. Brown (1913), who performed the first ileostomy for ulcerative colitis, and Logan (1919), who made a statistical study of 117 cases of ulcerative colitis. This was the largest series reported up to that time, and it included 13 post-mortem examinations, of which 3 showed ulceration of the terminal ileum. This paper appeared to stimulate interest in ulcerative colitis in America, for during the next six years many excellent publications were produced advocating surgical methods which were not adopted in this country for another ten to fifteen years. The pioneers who recommended ileostomy, colectomy, and ileorectal anastomosis for suitable cases of severe ulcerative colitis were Yeomans (1921), Stone (1923), Strauss, Friedman, and Block (1924), T. R. Brown (1925), and Rienhoff (1925). In this country Hurst (1921) and Rolleston (1922) made valuable clinico-pathological observations and also noted that the ileum in ulcerative colitis was rarely involved. Hern (1931) recognized ileal involvement, but considered its occurrence to be exceptional. Rankin, Bargen, and Buie (1932) stated that only late in the disease after repeated exacerbations would the ileocæcal valve be passed and the ileum involved. McKittrick and Miller (1935) found the terminal ileum involved in 1·3 per cent of their cases, but gave no indication as to how this figure was determined. Crohn and Berg (1938) stated that in regional colitis involving the cæcum and right colon the terminal ileum was almost invariably involved. They reported 13 cases, but gave no details regarding the extent of spread or the type of lesion found. Cattell (1939) noted an incidence of ileal involvement of 20 per cent; a considerable increase over previously published figures and probably to be accounted for by the fact that, for the first time, operation and not post-mortem specimens provided the basis for study. However, at a meeting of the

* Based on a thesis for the degree of Master of Surgery, University of London.

Royal Society of Medicine in 1953, Cattell stated that "over 10 per cent" of cases showed the ileum to be involved. Crandon, Kinney, and Walker (1944) reviewed the records of 16,500 consecutive post-mortem examinations carried out in Boston, and found 44 in which the primary cause of death had been ulcerative colitis; and of these, 39 per cent had ulcers in the ileum, which were generally confined to the terminal 12 in., though extending proximally for several feet in 3 cases. Dennis (1945) found that 33 per cent of patients with ulcerative colitis treated surgically had ileitis, and, in order to avoid making an ileostomy in a diseased portion of bowel, he advocated the removal of a segment of small intestine for examination, since it was not possible to detect the earlier changes of ileitis by external examination. In the same year Cave (1945) recognized retrograde spread to the ileum, but gave no indication of the incidence of this complication. Kirsner, Palmer, Maimon, and Ricketts (1948) observed that of 35 patients with ulcerative colitis having total involvement of the colon, 26 per cent had radiologically demonstrable involvement of the terminal ileum. Warren and Sommers (1948) found an incidence of ileal involvement of 25 per cent, but in the following year in their paper on the pathology of ulcerative colitis the figure had risen to 34 per cent. In 1949 McCready, Bargen, Dockerty, and Waugh described their experiences at the Mayo Clinic, and gave the only detailed account of the retrograde type of ileitis to be found in the literature. They studied 29 specimens of ulcerative colitis with ileal involvement which they had found in 81 post-mortem and 22 colectomy specimens. The incidence of small-bowel involvement was 28 per cent, and almost the same for both operation and post-mortem specimens. They found the average length of ileal involvement to be 20 cm., but in 7 cases discrete ulcers were present with normal intervening mucosa which extended over a greater length of the small bowel. The significance of this observation will be discussed later. They concluded that ileal involvement in ulcerative colitis might be an important factor in the high mortality-rate of ileostomy.

During this time there were very few references to ileal involvement in the British literature and at a meeting of the Medical Society of London in 1950 to discuss ulcerative colitis, no mention of ileitis was made.

Brooke (1954), in his monograph on ulcerative colitis, recognized that the retrograde spread of disease involved the ileum, but found only 4 instances in 57 cases of ulcerative colitis treated surgically—an incidence of 7 per cent. Warren and Sommers in the same year, as the result of examining more than 300 specimens which included both ulcerative colitis and Crohn's disease, came to the conclusion that the ileum was involved in 34 per cent of cases of ulcerative colitis.

Thus while there were considerable variations of opinion as to the incidence of ileal involvement in ulcerative colitis, the clinical significance of this complication was rarely considered.

ST. MARK'S HOSPITAL SERIES

Material and Methods.—During the three-year period ending in July, 1954, 130 total or subtotal (cæcum to lower sigmoid colon) colectomy specimens of ulcerative colitis have been examined in the Research Department of St. Mark's Hospital. Of these, 85 were primary colectomies, i.e., the colectomy and ileostomy were performed at the same operation; and the remaining 45 had been removed by a second-stage operation at varying times after a preliminary ileostomy. These two groups of primary and secondary operation specimens provided an opportunity to study the effect of rest in cases with ileal involvement. Twenty-three of these specimens were discarded because the ileum in each case was insufficient in length. The number finally selected for study was therefore 107, and consisted of 79 primary and 28 secondary colectomy specimens.

These were received from the operating theatre without having been opened. After the bowel had been washed free of fæcal material, the specimens were prepared by being gently filled with 10 per cent formol saline, sufficiently to restore their natural form; they were then submerged in a tank of formalin solution for two or three days (Dukes, Bussey, and Lamb, 1948). After fixation the bowel was bivalved and since the natural shape of the organ had been preserved, inspection and photography were more readily performed. A description of the gross characters of each specimen was made, and suitable areas selected for photography and section, and in this way a library of pathological records was established. The file on each case was completed by the inclusion of notes on the clinical history and surgical treatment.

Incidence of Ileal Involvement.—In 107 cases of ulcerative colitis there were 18 which showed complicating retrograde ileitis, giving an incidence of 17 per cent. These consisted of 13 examples of ileitis in 79 primary colectomies, and 5 in 28 secondary colectomies, showing incidences of 16 and 18 per cent respectively.

Age and Sex Incidence.—Of the 18 patients with ileal involvement, 10 were male. The patients were fairly evenly distributed over the second to fourth decades. The youngest patient was 16, and the oldest 73. With regard to age and sex incidence, therefore, the patients were representative of the whole group studied.

Ileal Involvement related to Clinical and Pathological Type of Ulcerative Colitis.—The case histories and general pathology of each specimen were studied in order to determine whether or not there was a clinical or pathological type of ulcerative colitis which tended to involve the ileum. It was found that the length of history varied from 4 months to 34 years. The patient with the 4-months' history had only slight ileal involvement confined to the terminal inch of the small intestine, and was of interest in showing how soon the change could develop. Although ileal lesions were more likely to be found in cases with longer histories, there was no definite relationship between the extent and severity of ileal disease and the length of history of ulcerative colitis.

Of greater significance was the associated clinical type of ulcerative colitis, for it was found that all the patients with retrograde ileitis had had either a chronic continuous, or a slightly remittent, type of disease without acute exacerbations. The same

question was studied in another way, for it was found that in the primary colectomy group of 70 patients there were approximately 40 per cent who had had exacerbations of ulcerative colitis of sufficient severity to endanger their lives, and that, of these, all except 4 showed well-marked pseudo-polyposis of the colon. There was thus no doubt of the relationship

FIG. 340.—Acute ulcerative colitis with competent ileocæcal valve and normal ileum.

between pseudo-polypi and the severity of attacks of ulcerative colitis, and it was therefore a most striking finding that none of the patients with ileal involvement had more than a minor degree of pseudo-polyposis.

It appeared that the acute fulminating form of the disease did not usually allow time for the ileum to be involved, and in many of the colectomy specimens from such cases, the sharply drawn line of demarcation at the ileocæcal valve between the dark, hæmorrhagic, cobblestone appearance of the cæcal mucosa and the pale normal ileal mucosa was most striking (*Fig.* 340). In nearly three-quarters of the cases in which the cæcum had been involved by ulcerative colitis, the ileocæcal valve appeared to present an effective barrier to the retrograde spread of the inflammatory process.

That involvement of the ileum was not a terminal event was shown by the tolerably good general condition of the majority of the patients, who with one exception survived their operations. The presence of ileal involvement therefore appeared to make no significant difference to the immediate prognosis.

Pathology.—

Macroscopic Features.—A variable degree of pathological change in the terminal ileum was found, both with regard to extent and severity, though generally the more severe the disease, the greater was the length of ileum involved. With the exception of 2 cases, in which the extent of the retrograde ileitis could not be determined because the bowel had been divided through a diseased area, the changes were confined to the terminal 14 in.

In 8 cases ileal involvement was confined to the terminal 4 in. of small intestine. These early cases were mainly of interest in indicating the mode of spread of ileitis, for in this group were found the only specimens which did not have obviously incompetent ileocæcal valves; 2 were competent and 2 others partly competent. It thus appeared that the destruction of the ileocæcal valve did not always precede the earliest ileal changes as had been suggested by Inberg (1953). However, the valve had been destroyed in all cases with severe involvement of the ileum, and often to such a degree that its position was difficult to determine.

Three grades of ileal pathology were recognized:

1. Slight—in which the mucosa appeared to be coarsely granular, with loss of valvulæ conniventes, but usually without ulceration, the changes being confined to the terminal 4 in. of ileum.

2. Moderate—in which the mucosa was granular and ulcerated, though occasionally this was difficult to see for the ulcers were sometimes pin-point in size. The changes were usually confined to the terminal 8 in. of ileum.

3. Severe—in this grade the mucosa was grossly distorted and in part destroyed, with severe ulceration and very occasionally a pseudo-polypoid arrangement of the surviving mucosal remnants. The bowel wall was slightly thickened and some degree of dilatation was commonly observed. These changes were confined to the terminal 14 in. of ileum.

By these criteria there were 8 slight, 5 moderately severe, and 5 severe cases of involvement of the terminal ileum.

It was interesting to note that there were no examples of severe involvement in the group of 23 second-stage colectomies. This probably indicated a general tendency towards healing of the secondary ileitis when reinfection from the colon and the trauma of the fæcal stream had been diminished or prevented, and microscopical evidence of healing was in fact present.

Although the wall of the ileum in the severe cases was 2–3 times thicker than normal, the bowel was usually somewhat dilated, and the general impression was quite unlike that presented by the thick-walled, rather stenosed bowel typical of regional ileitis. The regional lymph-glands were, however, markedly enlarged—a feature shared by both conditions although the histological characters were different.

The specimen illustrated in *Fig.* 341 typifies 'slight' ileal involvement. It shows a finely granular mucosa without ulceration but with some loss of mucous folds. Some cases classified as 'slight', however, with only the distal 1–2 in. of ileum involved show well-defined ulcers (*Fig.* 342). Whether or not ileal ulcers were present in the early stages seemed to depend largely upon the pattern of mucosal damage in the colon, for a very similar change was usually found in the ileum.

Histologically this stage was characterized by distortion of the mucosal crypts and flattening of the villi, the stroma being infiltrated by lymphocytes and plasma cells, and showing increased vascularity.

The muscularis mucosæ was thickened but intact, and the submucosa showed early fibrosis.

The case shown in *Fig.* 343 was typical of 'moderate' ileal involvement. The mucosa was more coarsely granular and showed multiple small superficial ulcers closely simulating the colonic pathology. Approximately 8 in. of bowel were involved, and the ileocæcal valve was widely patent and incompetent.

Histologically, small ulcers were present which did not extend beyond the muscularis mucosæ. The mucous membrane was infiltrated with inflammatory cells to such a degree as to cause distortion and partial blockage of some of the crypts, and this resulted in crypt abscess formation identical with that found in the colon in ulcerative colitis. The

FIG. 341.—An example of 'slight' ileal involvement.

FIG. 342.—An example of 'slight' ileal involvement with ulceration.

FIG. 343.—Showing 'moderate' ileal involvement. The arrow marks the site of the ileocæcal valve.

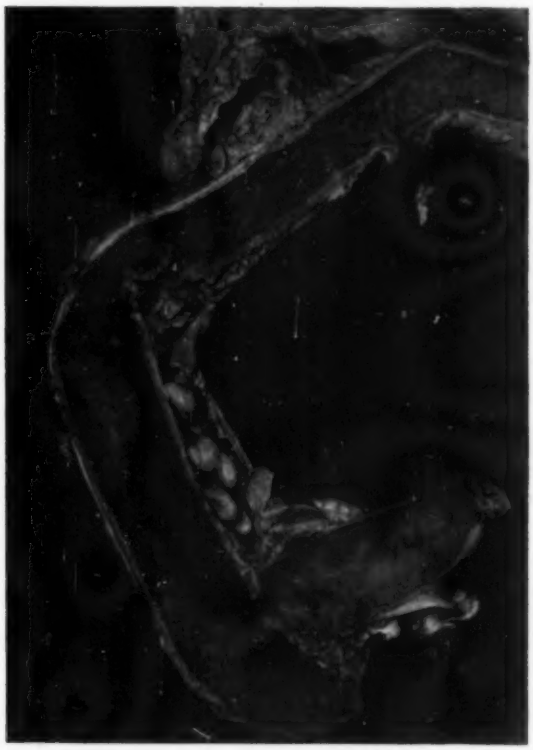


FIG. 344.—Another example of 'moderate' ileal involvement.

submucosa was slightly thickened, œdematous, and showed some increased fibrosis.

Fig. 344 illustrates a slightly less severe example of ileal involvement which shows pin-point ulceration and fine granularity of the mucosa. Although similar appearance. There was an abrupt transition from diseased to normal small intestine 14 in. from the ileocæcal valve, which though incompetent, was not completely destroyed as had been so commonly observed in cases of severe ileal involvement.

A B

FIG. 345.—A, ' Severe ' involvement of the ileum ; B, ' Close-up ' showing ileal pseudo-polypi and shallow ulcers.

FIG. 346.—' Colon-ization ' of the terminal ileum. The arrow marks the site of the ileocæcal valve.

FIG. 347.—' Severe ' ileitis with well-marked superficial ulceration. The arrow marks the site of the ileocæcal valve.

the ileum was abnormal at the site of section, the patient was in excellent health one year later, there being no sign of proximally spreading ileitis.

Fig. 345 illustrates a severe form of ileal involvement. The operation specimen consisted of the terminal 16 in. of ileum and the entire large bowel. The ileum showed some thickening of its wall, with a rough, granular, crinkled mucosa with a few scattered rounded pseudo-polypi, but no dilatation. The transverse colon showed a very

The histology of severe ileitis showed ulceration which extended into the superficial part of the submucosa. Many of the ulcers, however, were partly healed by regenerating flattened epithelium growing in from the periphery. The mucosa showed increased infiltration with lymphocytes and plasma cells, increased vascularity, deformation of crypts, and crypt abscesses, in a more striking way than had been seen in the previous specimens showing lesser degrees of severity. The pseudo-polypi consisted

of granulation tissue with a covering of flat atrophic epithelium.

Fig. 346 demonstrates to a remarkable degree ' colon-ization ' of the ileum with petechial hæmorrhages similarly disposed in both large and small bowel.

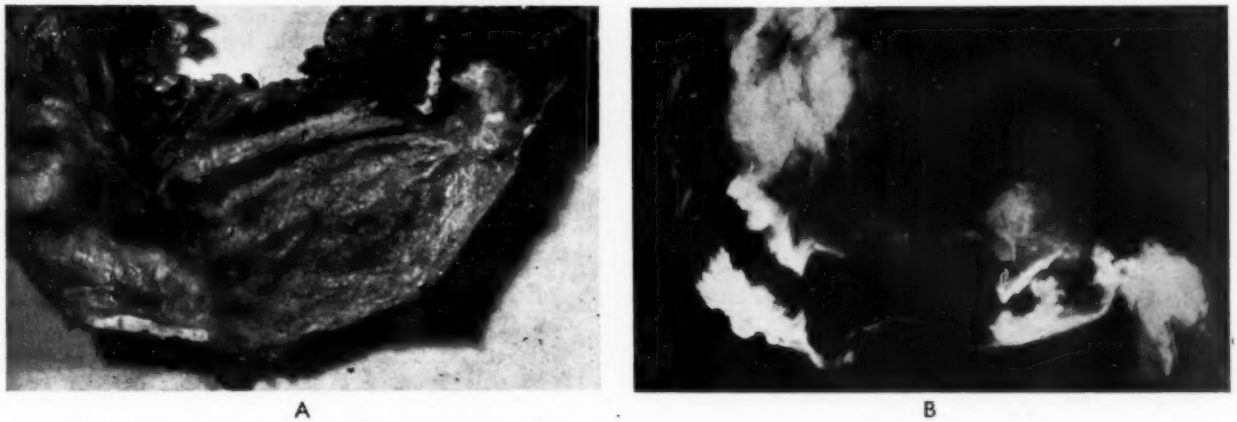
Histologically the mucosa showed minute ulcers and a dense round-cell infiltration. The ileum had been divided through an involved area and an ileorectal anastomosis performed. Six months later, although it was not possible to visualize the ileum satisfactorily by sigmoidoscopy, there was no clinical evidence of retrograde spread of ileitis, and a steady improvement in the general condition of the patient was observed.

Fig. 347 illustrates another example of ' severe ' ileitis, and the only one in which the ulceration appeared to be rather more marked in the ileum than in the colon. Once again the ileocæcal valve had been destroyed. This specimen was of further interest in that it also showed multiple adenocarcinomas of the left colon.

The example of severe ileal involvement illustrated in *Fig.* 348 showed enlargement of the regional lymph-nodes such as was commonly seen in the more severe forms of this complication. The involved area gradually merged into normal mucosa 12 in. above the ileocæcal valve. The histology was as before, with minute shallow ulcers. The lymph-nodes showed reactive hyperplasia only.

Fig. 349 A shows a healed retrograde ileitis nine years after a terminal ileostomy had been performed. The mucosa appeared to be smooth and atrophic and this was confirmed microscopically by its narrowness, the disappearance of the villi, and the wide irregular spacing of the crypts. The thin fragmented muscularis mucosæ and the thickened fibrotic submucosa also gave evidence of old inflammatory change. In addition to these changes, however, there were two areas of light coloured rather rubbery tissue which appeared to be infiltrating the submucosa—one immediately proximal to the ileocæcal valve, and the other 3–4 in. proximal to this. Microscopically these areas showed large numbers of phagocytic cells with a few foreign-body giant-cells filled with highly refractile particles. Radiography showed these areas to be densely radiopaque (*Fig.* 349 B). Dr. B. Lennox, of the Department of Pathology of the Postgraduate Medical School of London, extracted some of this refractile material, and by means of flame spectra found that it consisted of barium with a small amount of calcium. It was presumed that this remarkable specimen resulted from a barium enema performed while the bowel was ulcerated, phagocytosis and subsequent healing producing the result shown.

FIG. 348.—' Severe ' ileal involvement with enlarged regional lymphatic glands.



A B

FIG. 349.—A, Barium in submucosa of terminal ileum; B, Radiograph of terminal ileum showing radiopaque areas.

Radiological Findings.—Study of the radiographs of these cases revealed that only the more severe degrees of ileal involvement were demonstrable radiologically. Of the 5 cases classified as ' severe ', the 4 which had had barium radiography showed loss of mucosal pattern and sometimes slight dilatation of the ileum. None of the cases classified as slight or moderately severe showed radiological evidence of ileitis. McCready and others (1949) only demonstrated ileal involvement in about half

of their cases which subsequently proved either at operation or post-mortem examination to have had this complication.

In no case was it possible to determine the length of bowel involved with any degree of accuracy, although Kirsner and others (1948) in a radiological study of 89 cases of ulcerative colitis found that of 9 cases with retrograde ileitis 5 showed further spread of the condition when examined later. When a barium meal and follow-through had been carried out better visualization of the terminal ileum was achieved than by barium enema (*Fig.* 350).

FIG. 350.—Retrograde ileitis demonstrated by barium follow-through.

It was usually impossible to determine radiologically whether or not the ileocæcal valve was competent, for the weight of barium in the cæcum and ascending colon tended to force open the lips even of a normal valve.

Only in recent years has a preparation of barium been available, which, being compatible with body secretions, does not flocculate when in contact with gastric juice or mucus—this preparation consists of a thixotropic gelo-colloid which mechanically suspends colloidal-size particles of barium sulphate (Raybar). With this substance abnormalities of mucosal pattern in the terminal ileum can be more readily detected.

DISCUSSION

Ileal involvement in ulcerative colitis has been ascribed to 'backwash' through an incompetent ileocæcal valve, for the crescentic fold in which the ileocæcal valve is situated was obliterated in such cases by a combination of muscle spasm and later submucous fibrosis. Brooke (1954) pointed out that the lips of the ileocæcal valve were apposed in depth rather like the leaves of the mitral valve, and when flattened the valve was no longer competent. While all the specimens examined with incompetence of the ileocæcal valve showed varying degrees of ileal involvement, not all cases of ileal involvement were associated with incompetent ileocæcal valves, for in half of the cases with 'slight' retrograde ileitis the ileocæcal valves were relatively normal. It was probable, therefore, that in some cases the ileitis spread initially by direct continuity, and only later when the first inch or two of the ileum had been involved did the ileocæcal valve become incompetent. Retrograde spread of the ileitis was probably accelerated by the purulent fæcal colonic content—including possibly lysozyme from the pus cells (Sammons, 1951) which dissolved the protective mucus and rendered the ileal mucosa more susceptible to bacterial toxins.

The examples of ileitis found in the secondary colectomies had atrophic though intact mucous membranes with healed ulcers. How much of the healing was due to diminution of 'backwash' and how much to elimination of the trauma of the passage of fæces it was not possible to estimate.

With regard to the clinical significance of retrograde ileitis, a leading article in *The Lancet* (1951) on "Ulcerative Colitis with Ileal Involvement" stated: "It is not sufficient to leave examination of the small bowel until operation; for early mucosal changes, which increase and spread later, can be present before there is any alteration in the external appearance of the bowel wall."

McCready and others (1949) considered that ileal involvement was one of the commonest causes of mortality after ileostomy, and that the operation was contra-indicated unless it could be performed well above gross or microscopical involvement.

In both articles it was thought that retrograde ileitis continued to spread unless the diseased area was completely eradicated, and it has been generally considered that cases of ulcerative colitis with ileal involvement carried a worse prognosis than those without this complication. The present study, however, has shown that ileitis will heal after either colectomy and ileostomy or ileostomy alone, and that even when the ileostomy was made in a diseased area no harm resulted. The reason for the respect with which retrograde ileitis is regarded is believed to be due to its confusion with ileostomy dysfunction, a more dangerous condition which it superficially resembles. It is proposed to consider the differentiation of these two conditions in the next section.

Although in *The Lancet* article it was considered that examination of the ileum could not be left until operation, since radiology has been shown to be of limited value in determining either the presence or extent of ileal involvement, there would seem to be no other alternative. There are, however, three encouraging facts which may be emphasized by this study—first, ileal involvement was limited to 14 in. in over 100 cases of ulcerative colitis treated surgically; secondly, it is a simple matter, having divided the ileum, to inspect its mucosal surface and if necessary to section the bowel higher; and, thirdly, if the ileostomy be inadvertently made in a slightly diseased area no harm would probably result.

It is thus concluded that retrograde ileal involvement is a less serious condition than had been suspected in the past, and that this complication does not adversely influence the prognosis after surgical treatment.

ILEITIS SECONDARY TO ILEOSTOMY DYSFUNCTION

The second type of ileal lesion to be considered is that found in association with a subacutely obstructed ileostomy. Warren and McKittrick (1951), in an excellent paper, drew attention to the clinical picture which resulted from a stenosed ileostomy and found that it had occurred, though usually temporarily, in 62 per cent of their patients. That this form of subacute obstruction was very common in the early weeks following ileostomy was confirmed by Counsell and Goligher (1952), who found an incidence of 43 per cent in the St. Mark's Hospital cases.

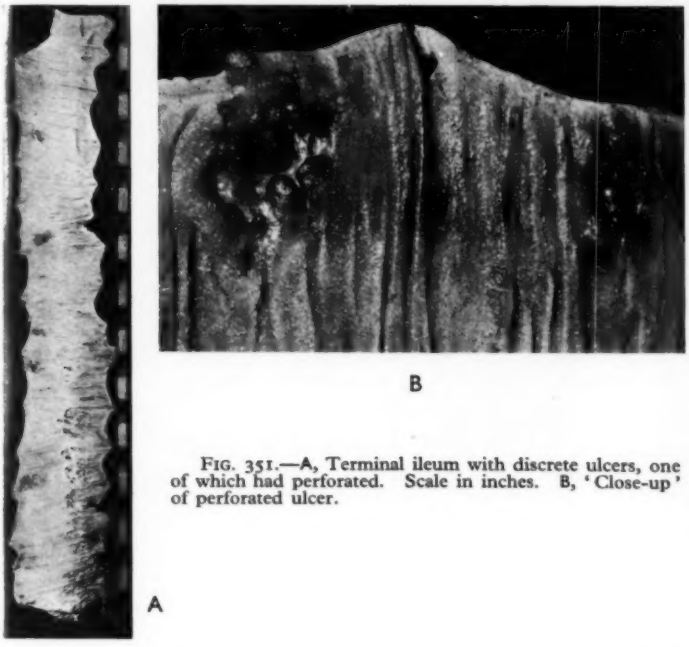


FIG. 351.—A, Terminal ileum with discrete ulcers, one of which had perforated. Scale in inches. B, 'Close-up' of perforated ulcer.

The condition was characterized by abdominal colic and paradoxically a profuse watery discharge from the ileostomy, with sometimes nausea and vomiting. The first systemic manifestation might be the sudden onset of a shock-like state, with peripheral circulatory failure, caused by profuse fluid and electrolyte loss.

Warren and McKittrick stated that there was an associated ulceration of the ileum proximal to the ileostomy, which had been demonstrated in 11 of their patients and evidenced by either perforation of the ileum or bleeding. However, no pathological details were given.

The correctness of this statement has been verified at St. Mark's Hospital as a result of this investigation, and it has further been demonstrated that this type of ulceration differed both macroscopically and microscopically from that found in retrograde ileitis complicating ulcerative colitis. Only the more serious cases with prolonged obstruction developed these changes, for the vast majority of patients recovered as a result of conservative measures such as dilatation of the ileostomy and catheterization.

Since the pathology of ileostomy dysfunction has not hitherto been described, it is proposed to give an account of the subject by quoting several illustrative cases, and later to compare and contrast retrograde ileitis with ileostomy dysfunction in the belief that these two conditions have been confused in the past. Such was the case with two patients treated at St. Mark's Hospital who have been recognized in retrospect as examples of 'dysfunction' after having been diagnosed as 'ileitis'.

Case 1.—Miss A. C., a receptionist aged 36 years, gave a five-year history of having passed blood and mucus in the stools, associated with mild diarrhœa. She had steadily lost strength for the previous nine months and had been confined to bed for most of this time. Weight 4 st. 10 lb. Hb 68 per cent. A terminal ileostomy with closure of the distal ileum was performed. The ileostomy subsequently functioned spasmodically and required repeated catheterization—the fæces remained fluid, and up to 3 l. a day were passed. Intermittent colicky abdominal pain and vomiting were followed by crises due to fluid and electrolyte imbalance which required parenteral saline solution. In spite of these measures the patient's general condition gradually deteriorated until symptoms and signs of peritonitis supervened suddenly 24 hours before death which occurred on the forty-first post-operative day.

POST-MORTEM FINDINGS.—An ulcer in the ileum approximately 3 ft. from the ileostomy had perforated and caused general peritonitis. The distal few inches of ileum were so friable and bound down by adhesions that they could not be removed. The small intestine immediately proximal to this is shown in *Fig.* 351 A, and examination revealed the presence of numerous shallow ulcers in the terminal 10 in., which were arranged in a linear manner tending to become confluent towards the ileostomy. A line of somewhat deeper discrete ulcers, having irregular ragged edges, and being separated from one another by apparently normal mucosa, were also observed more proximally. One of these ulcers had perforated (*Fig.* 351 B). The colon showed changes of ulcerative colitis, but no note was made regarding the condition of the ileostomy or of the defunctioned ileum.

Death was stated to be due to 'ileitis', and was recorded as such in papers on the surgical treatment of ulcerative colitis both by Gabriel (1952) and Counsell and Goligher (1952). At the time of the patient's death, ileostomy dysfunction had not been recognized as a clinical entity.

Case 2.—Mr. R. C., a turner, aged 37 years, had had diarrhœa associated with the passage of blood for five months. A terminal ileostomy had been performed elsewhere on account of progressive deterioration in his general condition. He had made good progress until the third post-operative week when complaint was made of colicky abdominal pain, associated with loud borborygmi and difficulty with the ileostomy. On one occasion after a period of inactivity, 84 oz. of watery fæces were discharged within a few hours, and catheterization of the ileostomy became necessary. After three weeks he was admitted to St. Mark's Hospital. Abdominal colic and intermittent fluid ileostomy actions associated with lower abdominal distension continued for ten days, after which time a subtotal colectomy was performed. At operation the exterior of the ileum proximal to the ileostomy looked normal, although it had been observed previously that a finger would not pass freely into the bowel, which appeared to be angulated at the abdominal wall. Post-operatively the colicky abdominal pain continued as before, and gastric aspirations of up to 4 l. a day alternated with periods of profuse watery ileostomy action. Parenteral fluids were given in large amounts

during this time. Three weeks after operation: Hb 94 per cent; plasma-protein 3·5 g./100 ml.; blood-urea 44 mg./100 ml. The patient's general condition gradually deteriorated and he died on the thirty-seventh post-operative day.

POST-MORTEM FINDINGS.—The terminal 9 in. of ileum were dilated and in this area the mucosa was ulcerated. Smaller isolated ulcers were also found proximally for a distance of about 4 ft. Examination of the colon removed by operation showed that the colitis was maximal in the descending and sigmoid regions, with little change other than slight granularity of the mucosa in the transverse colon, and a normal ascending colon and cæcum. This patient had been diagnosed as suffering from 'ileitis', although examination of the colectomy specimen showed that the ileostomy had been made in normal bowel.

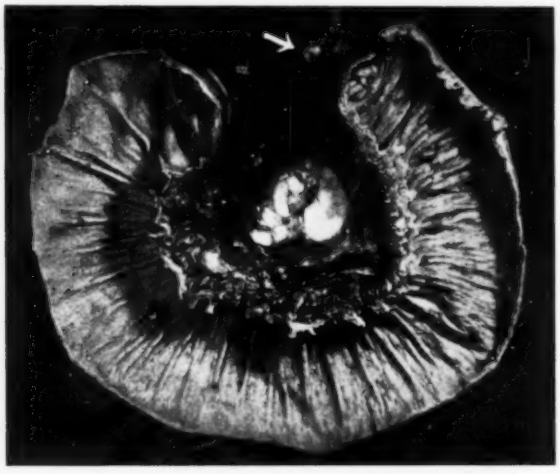


FIG. 352.—Ileostomy dysfunction showing discrete shallow ulcers. The arrow marks the ileostomy.

The next three St. Mark's Hospital cases differed from those already recorded in that they had been correctly diagnosed as ileostomy dysfunction. Each had had an ileostomy reconstruction performed when more conservative measures had failed to give relief.

Case 3.—Miss M. R., a schoolgirl aged 16 years, gave a six-year history of chronic diarrhœa and bleeding. Although she was pale and underdeveloped both physically and mentally and had not menstruated, her pre-operative health was relatively satisfactory. Primary colectomy with excision of the rectum and ileostomy was performed. The operation was followed by severe ileostomy dysfunction, which started in the second week and was manifested by abdominal colic, intermittent profuse watery ileostomy actions, and occasional vomiting. This condition persisted for two months, during which time both dilatation with Hegar's dilators, and excision of a fibrous ring at the mucocutaneous junction of the ileostomy had failed to relieve the obstruction. Several crises due to fluid and electrolyte loss had been overcome by massive transfusions of saline and dextrose solutions. The ileostomy was therefore remade, and at operation the terminal 11 in. of ileum were seen to be somewhat thickened and dilated; this segment of bowel was resected. The patient's subsequent course was uneventful and she was discharged from hospital 24 days later.

OPERATION SPECIMEN (*Fig.* 352).—Consisted of the terminal ileum ending in an ileostomy. The ileostomy was very tight and would not permit the insertion of the tip of the little finger. The distal mucosa was thickened and granular and showed irregular shallow ulceration which tended to become confluent near the ileostomy, and was arranged in a roughly linear manner. More proximally the ulcers were discrete and surrounded by normal mucosa. The mesenteric lymph-glands were greatly enlarged.

The colectomy specimen showed the typical changes of ulcerative colitis which were least severe in the ascending colon and cæcum (*see Fig.* 341). Although the terminal ileum was slightly involved by a retrograde ileitis, 9 in. of normal bowel had been resected proximal to this area, and the ileostomy had therefore originally been made in normal ileum.

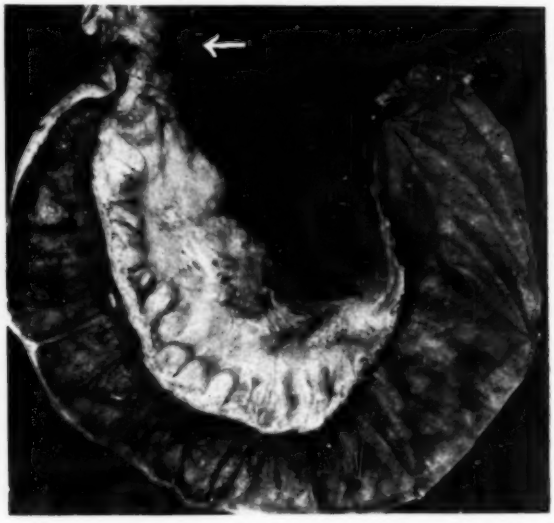


FIG. 353.—Ileostomy dysfunction with confluent ulcers distally and small discrete ulcers more proximally. The arrow indicates the ileostomy.

Case 4.—Mr. R. M., aged 20 years, had had a subtotal colectomy for ulcerative colitis with restoration of continuity by Devine's method. After one year perianal abscesses and fistulæ developed and it was necessary to re-establish the ileostomy. For four years the ileostomy functioned normally, after which time abdominal colic and fluid ileostomy actions started, and continued despite repeated dilatation, until the ileostomy was refashioned. All symptoms disappeared after this operation.

OPERATION SPECIMEN (*Fig.* 353).—This consisted of 16 in. of ileum terminating in an ileostomy which showed a severe degree of stenosis. Proximally the mucosa appeared to be normal, but more distally there were two groups of linear ulcers, on the mesenteric and antimesenteric borders, which tended to become confluent near the ileostomy. The ulceration immediately subjacent to the ileostomy may have been modified by the repeated passage of dilators. The regional lymphatic glands were enlarged and firm in consistency.

Case 5.—Mr. A. R., a labourer aged 50 years, had had a total colectomy including excision of the rectum for familial polyposis coli. The ileostomy worked satisfactorily for eighteen months, but after this time a mild degree of ileostomy dysfunction developed and it was found that the stoma would not admit a finger. The chafing of a badly fitting ileostomy appliance resulted in the formation of a fistula at skin level which accentuated the need for the ileostomy to be refashioned. At this operation the terminal 6 in. of ileum were resected.

OPERATION SPECIMEN (*Fig.* 354) showed changes similar to those previously described, although they were less well developed.

This case was of particular interest because the ulceration in the ileum developed after colectomy for a non-ulcerative condition of the bowel, namely familial polyposis coli.

Histology.—The 5 cases described were essentially similar though differing considerably in severity. Sections cut through the proximal parts of the small intestine were normal, but near the ileostomy shallow ulcers were seen with varying degrees of œdema and plasma-cell and lymphocytic infiltration of the submucosa. The granulation tissue forming the bases of the deep discrete ulcers in *Cases* 1 and 2 extended through the submucosa and muscle, the overlying subserous layer being densely cellular and œdematous. The general histological appearances of the discrete ulcers were similar to those seen in traumatic or stercoral ulceration, for the bowel surrounding the ulcers was relatively normal. There was thus no difficulty in distinguishing this condition from ulcerative colitis or Crohn's disease. The lymphatic glands showed chronic inflammatory changes of a non-specific character.

Research into the literature revealed that other cases had been described in which 'ileitis' had apparently developed proximal to an ileostomy. These cases were thought to have arisen as a result of the continuing retrograde spread of the disease, the ileostomy having been made in involved small bowel.

In 1944 Crandon and others reported the first cases of perforation of the ileum following ileostomy for ulcerative colitis. Two patients were described, both of whom had had severe ulcerative colitis for which ileostomy had been performed late in the course of the illness, after prolonged medical treatment failed to give relief. The post-operative courses of both patients were similarly marked by severe cramp-like abdominal pain, profuse fluid ileostomy action, and vomiting. At operation the terminal ileum of each patient appeared to be normal. Progressive deterioration was followed by death at 6 and 9 weeks after operation.

Post-mortem examinations revealed that death had resulted from peritonitis caused by perforation of ileal ulcers—6 cm. and 15 cm. proximal to the ileostomies. The extent of ileal ulceration was 15 cm. and 50 cm. respectively, and was described in one case as "a series of 15 small ulcerated areas in the mucosa", and in the other as "marked ulceration of the mucosa". The ileum of one was observed to be moderately distended. The author concluded that the colitis had spread into the ileum and caused ulceration, perforation, and death. There was no note as to the condition of the ileostomy stoma in either case. The clinical history and post-mortem findings were strikingly similar to those of the first two St. Mark's Hospital cases.

Olsan and Sussman (1948) described 4 post-mortem examinations of cases of ulcerative colitis in which the small bowel had been extensively involved. It was considered that the ileitis had resulted from retrograde extension of the ulcerative colitis. A significant fact was that 3 of these patients had had recent ileostomies, and although in 2 cases there were insufficient clinical details to determine whether or not there had been any ileostomy dysfunction, in the third case recurrent attacks of intestinal obstruction had been recognized. A further point of vital importance was the observation that in one of these cases the terminal ileum distal to the ileostomy had been normal.

Aetiology.—Warren and McKittrick (1951) believed the ulceration of the lower ileum in cases of ileostomy dysfunction to be due to hyperactivity and dilatation of the obstructed bowel, but it is difficult to accept this explanation since other forms of subacute small-bowel obstruction show no such tendency. Since the bowel content was invariably liquid in consistency, fæcal trauma could not have

FIG. 354.—A less severe example of ileostomy dysfunction. The arrow marks the skin level.

caused the changes even though a histological similarity to stercoral ulceration has been observed.

Another factor to be considered was malnutrition, for although, as already observed, the lesser degrees of ileostomy dysfunction were found in normally nourished patients, the severe forms of dysfunction associated with perforation only occurred in cases showing marked wasting, and the experimental work of McCarrison (1920), who produced ileal ulcers in monkeys as a result of dietary deficiency, would suggest that this was at least a partial explanation. However, De Nevasquez (1954), as a result of over 100 post-mortem examinations on the inmates of Belsen concentration camp, had shown that there was no tendency in human beings for small-bowel ulceration to occur in starvation. Thus although neither obstruction nor starvation alone could cause ulceration of the ileum in human beings, it is possible that a combination of these two factors might produce such a pathological state.

That ulceration of the ileum was not due to an inherent ulcerative diathesis which the small bowel might have shown in a lesser degree in ulcerative colitis, was demonstrated by the fact that the same changes developed proximal to a subacutely obstructed ileostomy in a case of familial polyposis coli.

Trauma caused by the passage of bougies and catheters could conceivably account for some of the changes in the immediate vicinity of the ileostomy, but not for the more proximal discrete ulcers.

DISCUSSION

The importance of ileostomy dysfunction has not been sufficiently recognized in the past for two reasons—first, the majority of mild cases recovered without surgical treatment and specimens were rarely obtained for study; and, secondly, as has already been suggested, the severe degree of ulceration found in fatal cases caused them to be diagnosed as 'ileitis'.

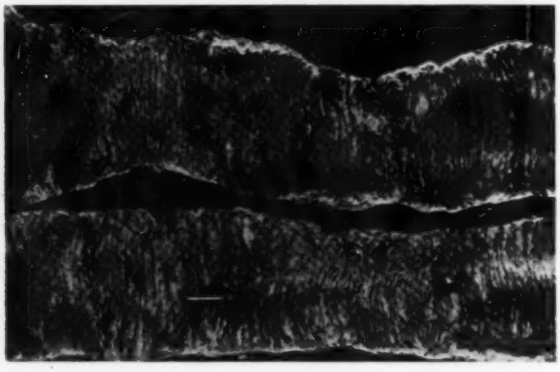


FIG. 355.—Illustration reproduced from the paper by McCready and others (1949), showing discrete ulcers in ileum; the quill marks an ulcer which had perforated.

It was apparent that the pathology of the first two cases differed only in degree from that of *Cases* 3, 4, and 5. Experience with this small group of patients indicated that the extent and depth of ulceration appeared to vary according to the general condition of the patient, and that perforation of the ileum was therefore unlikely to occur in the relatively fit patients who developed dysfunction several months after ileostomy, when well on the way to recovery. Only those who were toxic and had been ill for several weeks seemed liable to develop this complication.

The lesions found in cases of ileostomy dysfunction differed from those of retrograde ileitis complicating ulcerative colitis in several ways. In the latter condition the ulceration was shallow, and both macroscopically and microscopically closely resembled that seen in the colon. In this series the changes were limited to the terminal 14 in. of ileum.

By contrast, the ulceration resulting from ileostomy dysfunction, though tending to be confluent for a few inches immediately proximal to the ileostomy, was seen more proximally and typically in the form of discrete ulcers set in relatively normal mucosa. The ulcers were also found in a greater length of bowel than retrograde ileitis, particularly in severely ill patients, and histologically they resembled stercoral ulcers. In both conditions hyperplasia of the regional lymphatic glands was observed.

These findings were of particular interest in relation to the paper by McCready and others (1949), who noted two types of ileal involvement in ulcerative colitis, both ascribed to 'backwash' effects—a diffuse form resembling ulcerative colitis, and a form in which separate ulcers appeared intermittently in the ileum with the intervening portions of small intestine remaining essentially normal. *Fig.* 355 is reproduced from their paper and illustrates the discrete type of ulceration. This figure may be seen to bear a striking resemblance to *Fig.* 351 A, which was taken from a case of severe ileostomy dysfunction. The type of ileitis showing discrete ulceration was noted by McCready and his colleagues to involve a greater length of ileum than the diffuse type—another characteristic of ileitis due to ileostomy dysfunction. They also recorded a 17 per cent incidence of ileal perforation in cases with ileal involvement, though they did not state in which type of case this complication had been found.

This high incidence of perforation further suggested the incorporation of two pathological processes under one heading, for Rankin, Bargen, and Buie (1932), in reviewing nearly 700 cases of ulcerative colitis at the Mayo Clinic, though finding 23 cases of perforation, observed that all had occurred in the colon. The interesting feature of these statistics, and the probable explanation of the discrepancy between them, lies in the fact that while McCready's figures include a large number of patients who had had ileostomies and were liable to the complication of ileostomy dysfunction, Rankin's included relatively few.

A review of the literature revealed that perforation of the ileum was often associated with surgical intervention, and usually an ileostomy had been performed. Corbett (1945), in his Presidential address to the Proctological Section of the Royal Society of Medicine, reported 2 cases of ileal perforation, each of which had occurred proximally to an ileostomy and was thought to be due to the extension of ulcerative colitis into the ileum. One patient survived—no other record of survival after this complication has been found.

Jankelson, McClure, and Sweetsir (1945) observed 4 cases of ileal perforation—2 after ileostomy and 2 following laparotomy and handling of the bowel. Warren and McKittrick (1951), recording their experience of 240 patients with ulcerative colitis treated surgically, noted that 3 had died as a result of perforation of the ileum. The perforations followed the establishment of ileostomies in acutely ill patients, and in each case occurred proximal to the stoma.

These observations have led to the belief that perforation of the ileum is more likely to occur in severely ill patients with ileostomy dysfunction, than as a result of retrograde ileitis, for as has already been observed, retrograde ileitis is a superficial disease mainly confined to the mucosa and showing no tendency to perforation. It is also probable that ileal perforation is not associated with colonic perforation, for this complication occurs in the fulminating type of ulcerative colitis which rarely shows ileal involvement.

There were no instances of a retrograde type of ileitis developing proximal to an ileostomy in this St. Mark's Hospital series, and it was considered doubtful whether it ever occurred.

Prevention and Treatment of Ileostomy Dysfunction.—The daily measurement and charting of the ileostomy discharge has been found to be the most important safeguard against the insidious

development of ileostomy dysfunction, amounts over 30 oz. being viewed with suspicion.

The easy passage of a finger into the ileostomy does not exclude the diagnosis, for in a few patients the obstruction appears to be due to kinking of the ileum rather than stenosis at abdominal wall level.

There can be no doubt that errors in the technique of making an ileostomy account for most cases, and that the adoption of Brooke's (1954) method of suturing ileum to skin, and thus avoiding the formation of a ring of granulation tissue around the base of the ileostomy, has considerably diminished the incidence of this complication.

A small number of patients with ileostomy dysfunction who do not settle down within a few weeks as a result of dilatation and catheterization of the stoma require refashioning of the ileostomy. It is necessary to use a fresh segment of ileum, since local plastic procedures often fail.

REGIONAL ILEITIS COMBINED WITH ULCERATIVE COLITIS

The association between ulcerative colitis and regional ileitis (Crohn's disease) has not been universally recognized, for, while Crohn (1949) has stated that the two conditions were "probably members of the same family", and Johnson (1950), Lumb (1951), and Hinton (1952) have agreed with this view, Warren and Sommers (1954) considered the occasional finding of combined forms of the diseases to be due to coincidence.

There can, however, be no doubt of such an association, for the two conditions occurred in the same patient more commonly than could be explained by chance. This fact was demonstrated by the examination of Guy's Hospital statistics for the three-year period 1951–3, during which time 16 cases of Crohn's disease of the terminal ileum, and 60 cases of ulcerative colitis were found among nearly 25,000 admissions (excluding obstetric and pediatric cases). Thus roughly 1 case in 400 suffered from ulcerative colitis, and 1 case in 1500 from Crohn's disease. Although the chances of the two conditions occurring together in the same patient by coincidence would therefore be approximately 1 : 600,000, it was found that there were 3 cases of the combined disease in 130 specimens of ulcerative colitis examined in the Research Department at St. Mark's Hospital.

Review of Literature.—Lumb (1951), describing 27 cases of cicatrizing enterocolitis which included ulcerative colitis, Crohn's disease, and tuberculosis involving the right side of the colon, stressed the essentially similar clinico-pathological 'make-up' of regional enterocolitis and chronic ulcerative colitis.

Relatively few estimates of the incidence of coincident ulcerative colitis and regional ileitis could be found, but Crohn and Rosenak (1936) recorded 9 instances in 60 patients with regional ileitis, and Pemberton and Brown (1937) found a similar incidence in 39 cases of the same condition. Pugh (1945), in a smaller series, found that 12 per cent of cases with regional ileitis also had ulcerative colitis. Cave (1945) reported 7 cases of "inflammatory lesions of the small bowel resembling regional enteritis" in 80 cases of ulcerative colitis, thus showing an incidence of 13 per cent. Crohn (1949), recording the largest series up to that time, observed 22 cases of the combined disease in 306 cases of regional ileitis. Garlock, Crohn, Klein, and Yarnis (1951) had seen one patient develop ulcerative colitis after a two-stage ileocolonic resection for regional ileitis. In the discussion which followed this paper Cattell stated that associated ulcerative colitis and regional enteritis had been observed on "numerous occasions" and that sometimes the recurrence of symptoms following operations for regional ileitis was due to the development of ulcerative colitis. Hinton (1952) noted 3 cases of regional ileitis in 12 patients with ulcerative colitis. The figures of Cave and Hinton were higher than those found at St. Mark's and may well be due to confusion in nomenclature. For example, the term 'ileocolitis' had been employed by various authors to represent different pathological conditions, for while Bockus (1944) used the term for Crohn's disease of the terminal ileum and colon, to Warren and Sommers (1954) it was synonymous with the retrograde spread of ulcerative colitis into the ileum, while to Crohn (1949) 'ileocolitis' meant a combined form of ulcerative colitis and regional ileitis. Brooke and Cooke (1951) and Brooke (1953–4) have used the term for yet another condition which will be briefly discussed later.

In view of the rarity of combined ulcerative colitis and regional ileitis, it is proposed to describe a representative case—1 of the 3 which occurred in 120 patients who underwent colectomy for ulcerative colitis at St. Mark's Hospital.

CASE REPORT

Mr. L. B., aged 25 years, after having slightly loose stools for 6 years, suddenly became acutely ill with severe diarrhœa, pyrexia, and rapid loss of weight. E.S.R. 86. W.B.C. 21,000.

Sigmoidoscopy showed severe changes of ulcerative colitis with pseudo-polypi and ulceration, and a barium enema showed that the whole colon was similarly involved. Two months after the onset of the severe phase of his illness a colectomy and ileostomy were performed with an uneventful recovery.

The operation specimen shown in *Fig.* 356 A consisted of the colon to the mid-sigmoid region and the terminal 11 in. of small intestine. The large bowel showed acute generalized ulcerative colitis with an intensely congested, ulcerated mucosa studded with pseudo-polypi. The terminal ileum (*Fig.* 356 B) showed a thickened wall with some degree of contraction of the lumen and longitudinal ulceration of the mucosa. The ileocæcal valve appeared to be competent.

HISTOLOGY.—The wall of the ileum was greatly thickened and ulcers penetrating the muscle coat were seen. The thickened submucosa showed marked lymphatic hyperplasia without giant-cell systems.

The colonic histology was typical of severe acute ulcerative colitis and showed ulceration with the formation of many pseudo-polypi consisting of granulation tissue and remnants of mucosa.

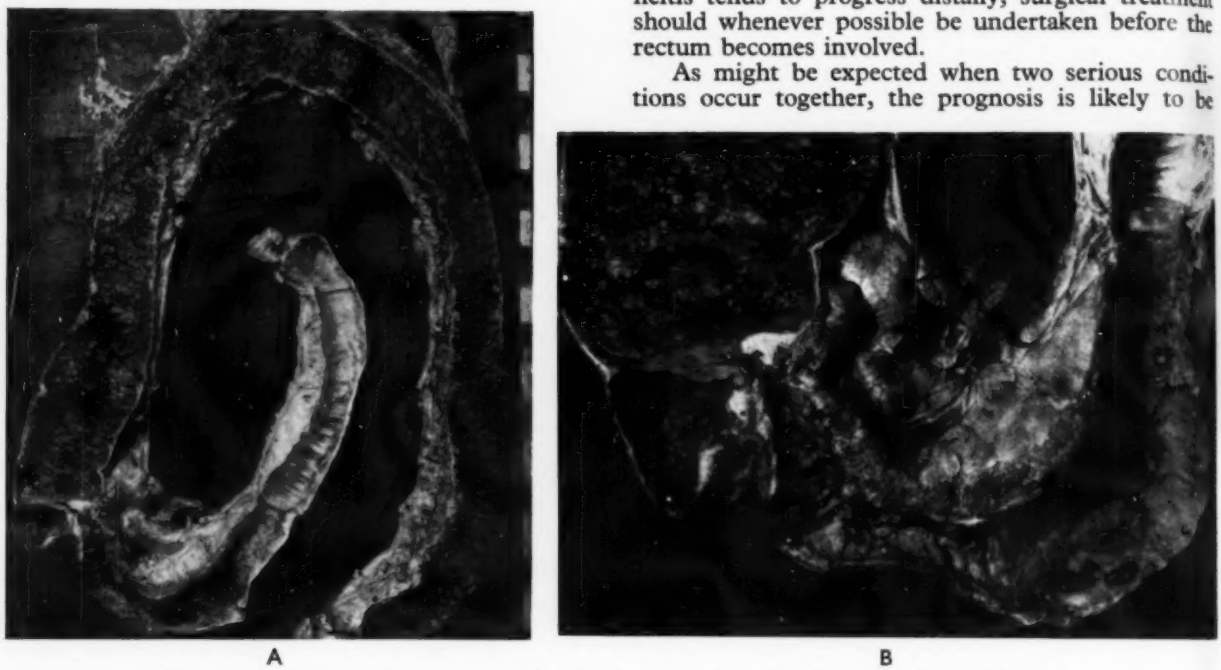
DISCUSSION

The association between ulcerative colitis and regional ileitis (Crohn's disease) has been confused by the fact that not only do these two conditions occur in the same patient, but that ulcerative colitis involves the ileum in about 15 per cent of cases, and regional ileitis sometimes involves the colon.

There are in addition certain clinical points of similarity between ulcerative colitis and Crohn's

disease, such as the age and sex incidence, the presence of anæmia, disturbances of nutrition, and associated rectal and perianal suppuration. Both conditions, too, show varying degrees of severity and extent of progression.

Although cases are occasionally seen showing microscopical features of both conditions, there is usually no difficulty in distinguishing retrograde or 'backwash' ileitis from regional ileitis found in conjunction with ulcerative colitis.



A B

FIG. 356.—A, Regional ileitis associated with acute ulcerative colitis. B, 'Close-up' of ileocæcal region.

The sequence of development when the two conditions are seen together is not known, but there is evidence to suggest that the regional ileitis usually arises first and is responsible for the secondary development of ulcerative colitis. For example, it is significant that whereas approximately 10 per cent of cases of Crohn's disease are followed by or associated with ulcerative colitis, the number of cases of regional ileitis arising in a similar series of ulcerative colitis cases is probably only in the region of 1–3 per cent.

The distribution of the colitis further suggests a primary lesion in the terminal ileum since most of these cases show maximal changes in the right colon, and often the rectum is not involved (Crohn, 1949).

The secondary nature of the colitis was commented on by both Crohn and Rosenak (1936), and Pemberton and Brown (1937), who noted that after the diseased ileum had been removed or following an ileocolostomy, the colonic lesions tended to heal. It has also been stated that after anastomoses between ileum and colon, although recurrences of Crohn's disease not infrequently arose in the ileum, they were rare in the colon (Crohn, 1949).

Although the aetiology of ulcerative colitis is unknown, it has been generally recognized that there may be predisposing factors, which acting on susceptible subjects might cause the disease. The factors suggested include bacillary or amœbic dysentery (Saundby, 1906; Hurst, 1921; Felsen, 1936); infections, particularly of the upper respiratory tract (Larsen, 1931); purgatives (Sloan, Bargen, and Baggenstoss, 1950); allergy (Andresen, 1925); and psychic trauma (Wittkower, 1938). Perhaps Crohn's disease should be added to this list.

Since ulcerative colitis associated with regional ileitis tends to progress distally, surgical treatment should whenever possible be undertaken before the rectum becomes involved.

As might be expected when two serious conditions occur together, the prognosis is likely to be bad. Crohn (1949) reported that 7 of 22 cases remained well although the period of follow-up was not stated, and Garlock and others (1951), after a 6-year follow-up, found that of 10 cases only 3 remained well. The 3 cases from St. Mark's Hospital have been operated on too recently for their follow-up to be of significance.

The histology of the colon in these 3 cases, although generally typical of ulcerative colitis, showed in 2 instances occasional giant-cell systems in the submucosa or muscle such as had not been observed in any of the 130 colectomy specimens of ulcerative colitis unassociated with regional ileitis, and there was thus a feature suggestive of Crohn's disease present.

Fig. 357 re-emphasizes the close association between ulcerative colitis and Crohn's disease, for in this case both conditions were found together in the colon, the former being represented by small shallow ulcers, the latter by two strictured areas. It was difficult to be certain whether the colitis was an atypical form of Crohn's disease, or ulcerative colitis, although histologically the latter pathology was suggested. It is, however, not always possible to make an unequivocal diagnosis in every case of the combined disease.

As suggested by Wells (1952), classification of ulcerative colitis and Crohn's disease should continue on a basis of descriptive pathology as long as their aetiology remains unknown.

ILEOCOLITIS

Brooke and Cooke (1951), in an article entitled "Ulcerative Colitis—a Diagnostic Problem and a Therapeutic Warning", described a condition in which it was suggested that a primary ileojejunitis caused secondary changes in the colon indistinguishable from ulcerative colitis.

Cooke's (1952) observation that sigmoidoscopy revealed a red velvety rectal mucosa which bled on slight trauma in some cases of steatorrhœa had

FIG. 357.—Combined Crohn's disease and ulcerative colitis of the colon.

originally suggested that this type of mild secondary colitis might in some cases become more severe, and ultimately simulate ulcerative colitis.

The diagnosis of 'ileocolitis' was considered in cases with mild persistent diarrhœa, without associated bleeding or the passage of pus until the later stages of colonic involvement, and confirmed by the demonstration of defective fat absorption, and changes in the terminal ileum revealed radiologically by the use of non-flocculating barium. Cooke (1952), however, found abnormal fat balance tests in 4 out of 20 patients with ulcerative colitis, and it has been established that barium meals will demonstrate only the more severe ileal lesions with certainty, and rarely give a precise indication of their extent.

'Right-sided' colitis was thought by Brooke and Cooke (1951) to be an early form of 'ileocolitis', at a stage before the inflammatory process had spread to involve the whole colon. However, not all cases of 'right-sided' colitis showed ileal involvement, for Crohn, Garlock, and Yarnis (1947) described 77 cases of regional ulcerative colitis of which 61 involved the right colon, and in 46 per cent of these cases the ileum was normal. There have been 4 cases of regional ulcerative colitis observed at St. Mark's Hospital during the last three years, 1 of which involved the cæcum; the ileum in this case was normal.

Whereas Brooke (1954) stated that the ileal lesions were essentially superficial and confined to the mucosa and thus distinguishable from Crohn's disease of the ileum, Cooke (1952) considered the condition to be a subacute form of this disease.

There was no pathological evidence for the existence of ileocolitis at the time of the original paper in 1951, and since that time only 2 specimens of the condition appear to have been obtained. (Cooke and Brooke, 1955.)

Brooke (1954) reported the incidence of retrograde ileitis to be only 7 per cent, less than half as common as 'ileocolitis' which was found in about 15 per cent of his 'colitis' patients. The sum total of these two types of ileitis approximates fairly closely to that found for retrograde ileitis alone at St. Mark's Hospital, and thus prompts the suggestion that perhaps some 'ileocolitis' patients might in fact be examples of severe retrograde ileitis.

St. Mark's Hospital exists primarily for patients requiring surgical treatment and therefore cases of idiopathic steatorrhœa are very rarely seen. Since Brooke and Cooke state, however, that the later stages of 'ileocolitis' and severe ulcerative colitis are clinically very similar and can only be distinguished from one another by radiological and biochemical means, it might be expected that some cases of 'ileocolitis' would have been observed. However, in the 5-year period ending in July, 1954, during which time more than 200 patients have been treated surgically for ulcerative colitis, no cases of 'ileocolitis' have been seen. There is, therefore, some doubt as to whether the condition occurs as frequently as has been suggested by Brooke and Cooke.

SUMMARY

Lesions of the ileum associated with ulcerative colitis were discussed under four headings :—

Retrograde Ileitis in Ulcerative Colitis.—

1. The presence of retrograde ileal involvement did not appear to influence the prognosis in ulcerative colitis.

2. The incidence of ileal involvement in 107 cases of ulcerative colitis was found to be 17 per cent. In the literature it had varied between 1 and 39 per cent.

3. This condition tended to complicate the chronic 'slow burning' type of ulcerative colitis as shown by the clinical history, the relative absence of associated colonic pseudo-polypi, and the greater average length of history before surgery was undertaken.

4. The ileocæcal valve was incompetent in all 'moderate' and 'severe' cases, and in half of the 'slight' cases. Incompetence did not, therefore, invariably precede ileal involvement as had been suggested.

5. The longest segment of ileal involvement was 14 in., although it seemed probable that had surgery been delayed the retrograde spread would have continued.

6. The ulcers, although varying in size, were always superficial in character and showed no tendency to perforate.

7. There were no obstructive lesions, for although the bowel wall was occasionally somewhat thickened, the lumen tended to be slightly dilated.

8. On the evidence of 2 cases, retrograde ileitis did not appear to progress after ileostomy and colectomy had been performed, even though a segment of diseased ileum was retained.

9. The ileum tended to heal after being bypassed, and there were no examples of severe involvement in the secondary colectomy specimens.

10. In the severe cases the regional lymphatic glands were enlarged, but showed only a non-specific inflammatory reaction.

11. Radiology could detect only severe changes in the ileum and gave little indication of the extent of such lesions.

Ileitis secondary to Ileostomy Dysfunction.—

1. The pathology of ileostomy dysfunction is described and its aetiology discussed.

2. It is suggested that in the past ileostomy dysfunction has been confused with retrograde ileitis, and the evidence for this belief is presented.

3. There were no instances of the retrograde type of ileitis developing proximal to an ileostomy, and it seems probable that this does not occur.

4. The prevention and treatment of ileostomy dysfunction is briefly discussed.

Regional Ileitis combined with Ulcerative Colitis.—

1. Three cases of regional ileitis combined with ulcerative colitis have been observed, one of which is described.

2. The association between ulcerative colitis and regional ileitis is discussed and the literature on the subject briefly reviewed.

3. The two conditions occur in the same patient more commonly than can be explained by coincidence.

4. When possible, surgical treatment should be undertaken before the rectum becomes involved.

Ileocolitis.—

No examples of 'ileocolitis' as described by Brooke and Cooke (1951) have been encountered in more than 200 cases of ulcerative colitis treated surgically at St. Mark's Hospital.

I am greatly indebted to the Surgeons of St. Mark's Hospital for allowing me to review their cases, and to Dr. Cuthbert Dukes for his kindness and encouragement. I acknowledge with thanks a grant received from the Research Department of St. Mark's Hospital.

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'MALIGNANT GRANULOMA' OF THE NASAL CAVITY

By H. G. RICHMOND, C. D. WEIR, *M.C.*, and J. F. PHILIP, Aberdeen

The designation of this disease indicates at once that its pathological nature, as well as its aetiology, is still unknown. Being usually fatal, 'malignant granuloma' is fortunately uncommon, although it is possible that additional cases have been reported under another name. We think it desirable to give an account of the clinical and pathological findings in another case which presented unusual and possibly significant features.

CASE REPORT

History.—A married woman, aged 44, complained of left-sided nasal obstruction of four months' duration. Examination of the nose showed a pale granular swelling of the left lateral nasal wall with considerable narrowing of the airway. On admission to hospital in April, 1954, the only additional feature was a little puffiness of the inner aspect of the left lower eyelid.

When a biopsy specimen was taken the inferior turbinate was found to be greatly expanded, the middle turbinate could not be defined, and on removal of tissue a firm gritty sensation was noted. The nasopharynx presented no abnormal appearance. The pathological report stated: "These fragments show highly cellular tissue with a rather granulomatous appearance. Mucous glands, presumably derived from nasal mucosa, are few in number but are diffusely scattered about in the tissue. The cellular component is pleomorphic, with small round cells, larger endothelioid cells, and spindle cells—both small and large. Thin-walled blood-vessels are fairly numerous. A striking feature is the degree of nuclear hyperchromasia of many of the cells and mitotic activity is fairly frequent. At first sight the appearances were those of a non-specific granuloma, there being no evidence of tuberculosis. However, the cellular picture gives such an impression of activity that the possibility of neoplasia has been considered. We incline to this view and consider that this case may well be an example of the extremely rare malignant granuloma of nose." The W.R. was negative. Radiography of the sinuses revealed obstruction of the left nasal cavity, with some haziness of the left frontal sinus. There was no evidence of abnormality of bone structure and the antra were clear. Oblique views of the ethmoid sinuses showed that the posterior ethmoidal cells on both sides were clear, and an occipito-mental view showed opacity of the left anterior ethmoid cells and of the left frontal sinus.

It was decided to treat the condition by deep X-ray therapy, and a surface dosage of 3150 r was given between May 4 and May 26. This diminished the granular mass in the nose and both the middle and inferior turbinates became definable. On May 29 the patient was allowed home.

Five weeks later she was re-admitted to hospital and, although the airway was now fairly clear and the nose showed no further formation of granulomatous tissue, there was œdema of both eyelids, with induration of the inner third of the lower lid. Further radiographs showed that the left frontal sinus and anterior ethmoidal region were now much clearer and that the posterior ethmoidal cells had remained clear. Biopsy of nasal tissue showed no evidence of the appearance found in the previous specimen. A week later, the eye lesion showed a mass of granulation tissue giving a firm broadened appearance to the lower lid with considerable surrounding œdema. A further report on a biopsy section from the granulations stated: "The appearance of one fragment indicates beyond any reasonable doubt that the lesion in the eyelid is of the same nature as the original lesion in the nose, namely, a malignant granuloma." A course of oral cortisone 25 mg. three times daily was given, with slight improvement initially.

By Aug. 15 the local appearance had become considerably worse, with puffiness and redness of the skin over the nasal bridge and with a margin of induration spreading across the midline. This deterioration was accompanied by severe headache, and it was decided to sacrifice the left eye to permit irradiation of the left orbit and nasal bridge. The enucleated eyeball was described: "In the superficial sclera near the corneoscleral junction there is a collection of pleomorphic cells which includes polymorphs, lymphocytes, plasma cells, histiocytes, and others of uncertain nature. Some cells with the morphology of plasmocytes are notably large. This exudate has several points of resemblance to that found in the nose in the original biopsy and is presumably part of the same process. It retains its atypical 'granulomatous appearance'." Deep X-radiation to a surface dose of 3000 r was completed by Sept. 8, the ulceration at the inner canthus then showing signs of healing. A rather low white-cell count was seen to be rising, and further radiographs showed no indication of breakdown of bone structure, when the patient was discharged home on Sept. 22.

On re-admission three weeks later with pyrexia, there was considerable nasal obstruction and a hard swelling had appeared over the left frontal sinus, with surrounding tenderness. The skin over this swelling was hot to touch. The lids were œdematous and a deep ulcer at the inner canthus, 2·0 cm. in diameter, had necrotic edges with a sloughing base. The results of swab culture and sensitivity tests suggested the use of particular antibiotics and several were tried systemically along with local dressings of various kinds. An extensor plantar response was noted on Sept. 21 and about this time the local lesion flared up after showing some signs of settling. The urine, previously negative, now had a trace of albumin. Severe headache and vomiting made their appearance, accompanied by extreme depression. Neurological examination showed quite definite signs of invasion of the C.N.S.: either metastasis or abscess, probably in the left frontal region.

Again a brief temporary improvement was followed by further signs of relentless local progress of the lesion, when the appearance was as illustrated by *Fig.* 358, and during the following week a black necrotic edge to the ulcer appeared along with a distressing deterioration in the general condition. The abdomen became distended, signs of subacute peritonitis were present, and the urine was by now foul-smelling. A menstrual period had continued for a month or more, but a gynæcological examination showed no abnormality in the pelvis. The abdominal distension increased in the last few days, till death took place on Nov. 16.

At Autopsy.—Post-mortem examination was carried out two hours after death. The notable external features were emaciation and the gangrenous lesion in the left orbit depicted in *Fig.* 358.

Head: The orbital plate of the ethmoid on the left side was eroded and the mass filling the left orbit was in direct continuity with fleshy, partly necrotic tissue in the ethmoidal sinuses and left frontal sinus. Small polypoid growths extended through the cribriform plate to involve the inferior aspect of both frontal lobes of the brain. The turbinates on the left side were swollen, but there was no evidence of infiltration of the floor of the nose.

The left maxillary antrum and the sphenoidal sinus were clear.

Examination of the brain showed congestion and softening of the inferior surfaces of both frontal lobes extending 2·5 cm. and 1 cm. into the substance on the left and right side respectively (*Fig.* 359).

Chest: A small, pale, firm subpleural nodule of tissue (1 cm. across) was noted in the right upper lobe. A

FIG. 358.—The appearance of the lesion just before death.

larger subpleural mass of tissue (4 cm. across) was found in the middle portion of the right lower lobe, and the cut surface appeared pale-red and yellow.

The heart showed a mild mitral stenosis.

Abdomen: A slight excess of serous fluid was present in the peritoneal sac. The gastro-intestinal tract was normal apart from the large bowel. Much gaseous distension of the large bowel was present and examination of the wall showed numerous small, slightly raised, yellow plaques on the mucosa of the transverse and sigmoid colon with occasional superficial ulcerations.

The liver, gall-bladder, spleen, pancreas, adrenals, and lymph-nodes were normal.

The kidneys showed the features of an old pyelonephritis.

The left ovary was normal in size. The right ovary was enlarged to about three times normal. Both showed areas of hæmorrhage and yellow areas of necrosis, the right ovary being more conspicuously affected.

Mild atheromatous changes were noted in the aorta.

The left common iliac vein was partially obliterated and contained adherent thrombus.

HISTOLOGICAL REPORT.—

Mass in Left Orbit: Much of this mass was necrotic, but it consisted of fibro-fatty and muscular tissue widely infiltrated by cells (*Fig.* 360), the ghosts of which were still apparent. Thrombosis was noted in numerous vessels. Where necrosis had not yet supervened the character of the cellular infiltrate could be demonstrated. In many areas the majority of the cells resembled reticulum cells and a substantial number of them were large and aberrant, binucleate and multinucleate forms being seen. The nuclei of some of these cells were hyperchromatic and mitoses were frequent, although in general there were not more than two mitoses per high-power field. Other cell types included lymphocytes, foamy macrophages, and neutrophil polymorphonuclear leucocytes. Sudanophilic material was present in the macrophages around pre-existing fat cells. Neutrophil polymorphonuclear leucocytes were particularly seen at the edge of necrotic areas. Gram staining showed degenerate cocci on the ulcerating surface.

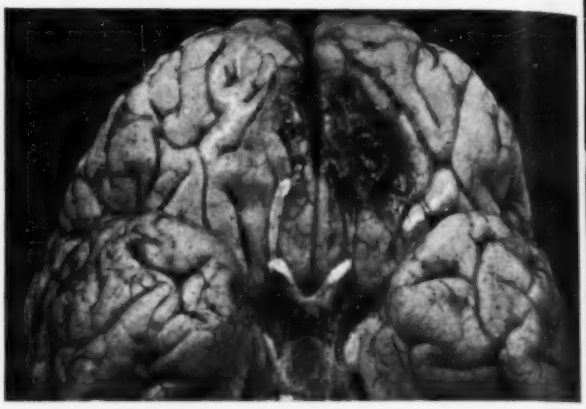

FIG. 359.—Congested softened under-surfaces of frontal lobes, more marked on the left side.

FIG. 360.—Section from mass in orbit. Note the highly cellular tissue invading muscle-fibres. (× 75.)

Brain: Microscopical examination of the lesion in the left frontal lobe revealed a superficial area of necrosis with underlying œdema and hæmorrhage. Thrombosis was present in the overlying veins and in one venule a peculiar cellular infiltration of the intima by histiocytes was seen (*Fig.* 361).

Lung: The large lesion in the right lower lobe was an area of necrosis supervening on a cellular exudation into the alveoli. Thrombus was seen in the related arteries. At the viable edges of the lesion, the cellular infiltrate included histiocytes—many foamy in type—round cells, neutrophil polymorphonuclear leucocytes, but also conspicuous numbers of large and aberrant reticulum cells in which mitoses were not infrequent.

The appearances were therefore similar to those seen in the orbit.

Ovaries: Both ovaries showed a pleomorphic cellular infiltration, more extensive in the right ovary, the tissue being highly vascular and showing extensive necrosis in some areas. The most conspicuous feature was the presence of large bizarre reticulum cells in which up to four mitoses per high-power field could be seen. Large multinucleate reticulum cells extended into the normal ovarian stroma at the periphery of the lesion. (*Figs.* 362, 363.)

Tissue around Thyroid: The fat around the thyroid showed a focus of cellular infiltration indistinguishable from that seen in the ovaries.

Colon: The lesions in the colon were superficial erosions showing secondary infection. There was underlying œdema and fibrinous exudate, and occasional multinucleate cells were present.

Lymph-nodes (Cervical, Bronchial, Cœliac), Spleen, and Bone-marrow: There was no disturbance of the normal architecture of the lymph-nodes and spleen. Red-cell and white-cell precursors were present in normal amounts in the marrow, but an increase in reticulum cells was evident.

Other tissues examined included stomach, pituitary, adrenals, thyroid, pancreas, uterus, liver, kidneys, and abdominal skin. No contributory features were noted in these organs.

DISCUSSION

Opinion is sharply divided with regard to the pathogenesis of 'malignant granuloma', whether it is allergic, infective, or neoplastic. The chief proponents of the allergic theory are Klinge (1933), Wegener (1939), Teilum (1946), and Williams (1949). An infective origin is put forward by Stewart (1933), Hoover (1941), and Sneddon and Colquhoun (1952),

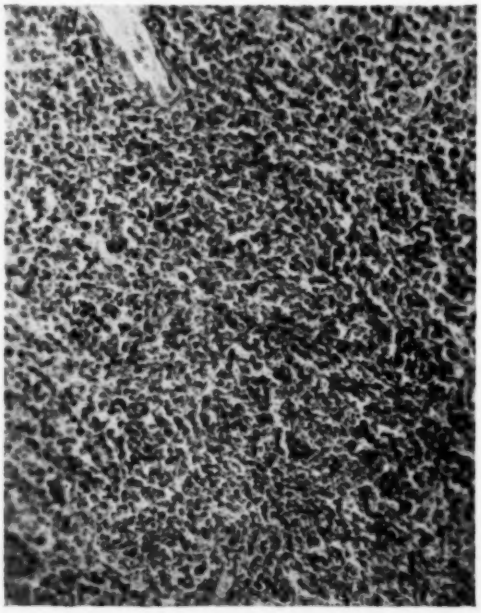

FIG. 362.—Section to show great cellularity of the tissue infiltrating the left ovary. Pleomorphism can also be appreciated at this magnification. (× 100.)

while cases with neoplastic characteristics have been recorded by Kraus (1929), Hall (1934), Greifenstein (1937), Shutz (1938), and Pirodda and Guenzi (1950).

In our case the macroscopical and microscopical appearances are those of a locally destructive and invasive lesion in the nose, orbit, and brain, with

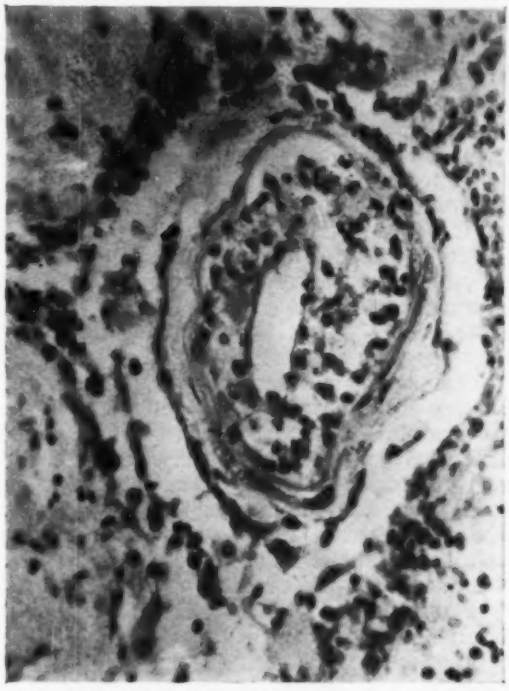

FIG. 361.—Gross intimal thickening of a venule in the region of the left frontal lobe lesion. This thickening is largely due to an infiltration by histiocytic cells. (× 283.)

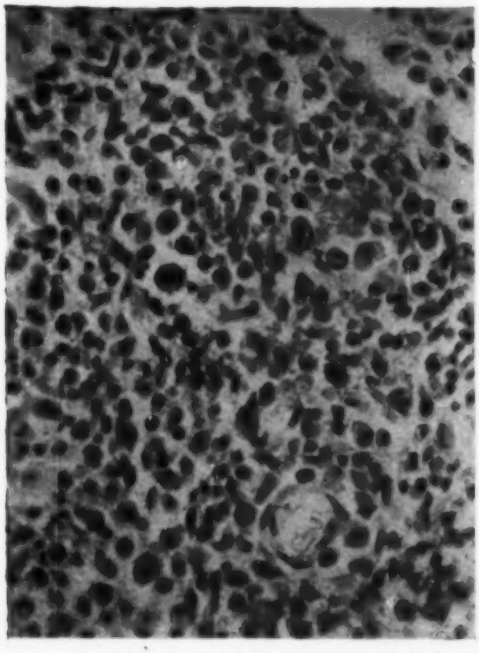

FIG. 363.—High-power view of infiltrate in left ovary. Many of the cells are reticulum cells showing irregularity in nuclear size and chromatin content, binucleate forms, and mitotic activity. (× 283.)

metastatic deposits in the lung, ovaries, and tissues of the neck. The most notable microscopical feature is a proliferation of reticulum cells, many of which are large multinucleate. Whilst occasional aberrant

reticulum cells may be found in many cases of inflammation, the picture here is too widespread and dominant to be regarded as a manifestation of any ordinary inflammatory process. Macrophages and neutrophil polymorphonuclear leucocytes are often seen in abundance in association with areas of necrosis and therefore may represent a secondary feature.

The appearance of the reticulum cells is essentially that seen in Hodgkin's disease—e.g., giant bizarre forms, mirror-image cells. Fibrosis, however, is not conspicuous and eosinophil leucocytes are absent, so that it would be inappropriate to regard the condition as an established example of Hodgkin's disease. It is noteworthy that there has not been a general involvement of the reticulo-endothelial system other than the non-specific changes already noted.

Vascular changes, characterized by thrombosis and occasionally a peculiar form of endarteritis (*Fig.* 361) are essentially local phenomena in the areas of neoplastic tissue. There was no evidence of polyarteritis or similar lesions elsewhere in the body, as described in several cases reported as belonging to the malignant granuloma group. However, as we have had experience of a case of polyarteritis presenting as a lesion in the nasal mucosa in which biopsy and later autopsy were carried out, we think that this type of ulceration of the nasal cavity should be placed in a separate category.

Spontaneous remission of varying degree and duration is not unknown in malignant disease, especially in the reticuloses, and in its behaviour malignant granuloma has many characteristics suggestive more of an atypical reticulosis than of an infection, not only by its response to radiotherapy (Howells, 1955; Glass, 1955; and Ellis, 1955), but by its failure to respond to antibiotics except in the case recorded by Sneddon and Colquhoun (1952) for which unfortunately no biopsy report is available. The response to cortisone obtained by Moore, Beard, Thoburn, and Williams (1951), and to ACTH by Hagens, Parry, and Markson (1953), has been short (one month and seven months respectively) and such responses are not uncommon in reticulosis and certainly do not support the theory of allergy to the exclusion of new growth.

The concept of malignant granuloma as a tumour of the reticulo-endothelial system can be compared to the occurrence of extramedullary plasma-cell tumour originating in the nasal cavity. In the review by Hellwig (1943) certain cases he described as plasmocytoma showed the presence of immature cells of lymphoblastic type.

From our own observations and a review of the literature we regard malignant granuloma as a variant of reticulum-cell neoplasia.

If our interpretation is correct then it provides a rationale for the empirical use of radiotherapy, which Ellis (1955) found successful in his first case. It would also explain the temporary benefit occasionally obtained by the use of cortisone and ACTH.

SUMMARY

A case of malignant granuloma of the nose and orbit is reported. The clinical and pathological features suggest that the condition is neoplastic and not infective in origin.

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LONG-TERM SURVIVAL AFTER PANCREATECTOMY FOR CANCER

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THERE is a fairly widespread belief that pancreatectomy for cancer is an operation offering a very high immediate mortality and an almost negligible chance of long-term survival. Experience suggests that this attitude of unqualified gloom is not justified, at any rate in the case of some varieties of malignant tumour. Muir (1955) has recently reported 2 cases of 5-year survival after pancreatoduodenectomy. It is important that cases of this kind should be reported in order to make it clear that patients who have undergone a major pancreatic resection may sometimes live for years in a normal state of health.

Between 1946 and the present time the writer has performed 57 pancreatic resections, 38 of them for cancer. Of these latter, 3 patients died in the immediate post-operative period, a mortality of 7·7 per cent. The details are shown in *Tables I* and *II*. In fact, the 3 who died were among the first 5 patients with cancer treated by pancreatoduodenectomy and there has been no mortality in the last 33 operations of this kind. In at least 2 of the 3

fatal cases the fault was one of selection and in similar circumstances to-day resection would not be performed (e.g., in one case the patient was a lady

Table I.—PANCREATECTOMY FOR CANCER: OPERATIVE MORTALITY

	Cases	*Deaths*	*Mortality* per cent
Pancreatoduodenectomy	34	3	8·7
Transduodenal resection of ampullary carcinoma	1	0	0
Distal pancreatectomy for cystadenocarcinoma	1	0	0
Gastro-colo-pancreatectomy for sarcoma of the pancreas	1	0	0
Subtotal pancreatectomy for multiple islet-cell carcinomata	1	0	0
Total	38	3	7·7

who before her illness weighed 18 st. and had a carcinoma of the head of the pancreas infiltrating the pyloric antrum. A palliative operation should have been preferred to pancreatoduodenectomy).

Table II.—CASES TREATED BY PANCREATODUODENECTOMY

	Cases	*Deaths*	*Mortality* per cent
Carcinoma of the head of the pancreas	9	3	33·3
Carcinoma of the ampulla of Vater or duodenum	25	0	0
Total	34	3	8·7

Provided then, that resection is carried out only in suitable cases, it can be performed with a very low immediate mortality.

LONG-TERM RESULTS

Twelve patients operated upon before July, 1951 qualify for 5-year assessment. Six of these lived for five years or more :—

Case 1.—**Carcinoma of the duodenum.**

Mrs. E., aged 62, had in the past suffered periodic attacks of abdominal pain diagnosed as biliary colic. In the summer of 1947 she began to complain of increasing flatulence and vomiting and in August she became jaundiced, and this deepened progressively until a surgical opinion was sought in November. By this time she had lost 2 st. in weight and complained of marked lassitude and anorexia. The most important physical finding was an easily palpable gall-bladder. After routine preparation, laparotomy disclosed a stenosing carcinoma of the second part of the duodenum, obstructing the common bile-duct and invading the pancreas. One-stage pancreatoduodenectomy was performed and was followed by an uneventful convalescence. Histological examination confirmed a primary carcinoma of the duodenum. The patient has been seen at intervals since and underwent thyroidectomy for a nodular goitre 1 year ago. She remains in good health, now nearly 9 years after pancreatoduodenectomy.

Case 2.—**Carcinoma of the duodenum.**

C. W., a man of 70, was explored in January, 1949, on account of duodenal obstruction for several months followed by jaundice for 2 weeks, with a palpable gall-bladder. A stenosing duodenal carcinoma was found and one-stage pancreatoduodenectomy was performed. Convalescence was uneventful. He died at home in July, 1955, of 'pneumonia', pulmonary metastasis clearly being a possibility, though this was not considered to be the cause of death.

Case 3.—**Cystadenocarcinoma of the pancreas.**

I. H., a man of 48, was operated upon for a huge cystadenocarcinoma of the body and tail of the pancreas in October, 1950, resection necessitating a thoraco-abdominal incision. Full clinical details have already been recorded elsewhere (Rodney Smith, 1953).

Post-operatively there was a temporary leakage of pancreatic juice for a week or two, and possibly due to this a ventral hernia developed. This was successfully repaired in 1955.

The patient remains in excellent health in July, 1956, 5¾ years after resection.

Case 4.—**Ampullary carcinoma.**

J. R., a man of 65, was admitted to hospital in December, 1950, with 3 weeks' deepening obstructive jaundice, anorexia, and loss of weight. A palpable gall-bladder was found on examination.

Laparotomy revealed an ulcerating ampullary carcinoma without metastases. One-stage pancreatoduodenectomy was performed. Convalescence was complicated by a temporary leakage of bile, but the patient was nevertheless able to leave hospital after 3½ weeks. He remains well 5½ years after resection.

Case 5.—**Ampullary carcinoma.**

M. C., a lady of 72, was admitted to hospital in May, 1951, with a 4 weeks' history of obstructive jaundice, anorexia, loss of weight, and steatorrhœa. The gall-bladder was not palpable. After routine investigation and preparation, exploration disclosed an ampullary carcinoma. One-stage pancreatoduodenectomy was followed by an uneventful convalescence.

The patient is in good health 5 years after operation.

Case 6.—**Ampullary carcinoma.**

J. P., a man of 52, was investigated on account of obstructive jaundice, abdominal pain, and loss of weight, associated with a marked degree of anæmia and occult blood in the stools. At operation the ampulla was found to be replaced by a malignant ulcer about 1 in. in diameter. One-stage pancreatoduodenectomy was performed. Convalescence was complicated by leakage of bile-stained fluid for 2 weeks, but recovery was never in doubt and the patient left hospital after 3 weeks. He remains well just 5 years after operation.

COMMENT

A particular interest in pancreatic surgery during the great expansion in this field of the last ten years has allowed certain conclusions to be drawn about the place of surgery in malignant obstruction of the lower common bile-duct.

1. Patients with malignant obstructive jaundice should be explored and a prognosis of unqualified gloom is not justified.

2. Carcinoma of the pancreas means a difficult resection with a significant operative mortality, followed by a very poor long-term prognosis even if excision is possible. In most cases palliative biliary short-circuit is the procedure of choice.

3. Carcinoma of the ampulla of Vater means a much easier resection with a low mortality, followed by a favourable long-term prognosis. Many of these less highly malignant lesions appear to be primary carcinomas of the *duodenum*.

4. Carcinoma of the common bile-duct in the pancreatic groove appears to carry an intermediate prognosis between these two types. The operation can be carried out without undue technical difficulty, but the chances of early hepatic metastases are higher than after resection for ampullary carcinoma.

5. If resection is to be performed, a one-stage procedure is usually best. In the very ill, very jaundiced patient, if two-stage resection is considered right, the best first stage is probably cholecystostomy through an incision laterally placed, well away from the incision later used for resection.

6. Some idea of the type of growth present may be gained before operation. Severe pain, particularly backache, usually means a fixed pancreatic growth and inoperability.

7. At operation, it is not always easy to be certain what type of growth is present or even if there is a growth at all. Surface biopsy of the pancreas must not be contemplated. Transduodenal exposure of the ampullary region and, if necessary, transduodenal biopsy should be performed if real doubt exists, but as this procedure has been followed by recurrence of growth in the wound, presumably locally implanted, exposure and handling of the ulcerating tumour surface is best avoided when possible.

SUMMARY

Six cases of 5-year survival after pancreatic resection for cancer are reported.

Some conclusions about the indications for this operation are described.

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HYPOTHERMIA: A METHOD OF INTRAGASTRIC COOLING

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FOR centuries the heart was thought to be so delicate that the slightest injury to it would be fatal. Both Billroth and Sir James Paget declared that the heart lay outside the sphere of surgery.

From 1895 to 1913 the experimental work of Del Vecchio, Haecker, Schepelmann, Elsberg, Carrel, and many others revealed that the heart could tolerate surgical trauma. On the other hand, the medical tradition of centuries was not easily set aside, and for 25 years more the treatment of acute trauma was the only clinical application of this knowledge.

In 1938 Hubbard, a pædiatrician, persuaded Robert Gross to operate on a child suffering from a patent ductus arteriosus (Gross and Hubbard, 1939). The success of the operation clearly indicated that the heart was not unique among the organs of the body; it, too, was amenable to surgical therapy.

Since the beginning of this century the possibilities of operations on the human heart have been explored. The scope of cardiac surgery, however, was at first confined mainly to the pericardium and neighbouring great vessels, or to the exterior of the heart chambers.

More recently the surgical field has been extended to the interior of the chambers of the heart, but in almost all instances the manœuvres have been done blindly, guided only by the feel of the palpating finger or the introduced surgical instrument. Although there are many recognized blind procedures, a fundamental principle of good surgery is to obtain a clear view of the field of operation and in this regard the exposure of the interior of the heart has set some unique technical problems. Ideally, to overcome these the circulation through the heart must be interrupted for a period of time. The solution to this problem has been investigated along two separate lines.

The first and more obvious method is to by-pass the heart by an artificial circulation. This is best achieved by an extracorporeal heart–lung machine (Gibbon (1937, 1939), Björk (1948), Dennis, Karlsen, Eder, Nelson, Eddy, and Sanderson (1951), Miller, Gibbon, and Gibbon (1951), Melrose (1953)) with temporary exclusion of the heart from the circulation. The technical difficulties associated with this problem are great, namely:—

1. Instruments are complex and costly.

2. Major operative procedures are required to attach the machine to, and later remove it from, the patient's circulatory system.

3. Blood must be heparinized and its ability to clot later restored with protamine.

4. Overloading of the circulation must be avoided.

5. Hæmolysis of the blood and the leak of air into the circuit must be guarded against.

6. Blood-flow from the coronary sinuses into the right atrium obscures the operating field.

The second approach to the 'bloodless heart' has been to reduce cellular metabolism by lowering the body temperature until the cells can withstand prolonged periods of ischæmia. The circulation can then be interrupted for a sufficiently long period to perform intracardiac reconstructive operations. This is the main application of hypothermia.

METHODS OF INDUCING HYPOTHERMIA

1. Surface Cooling.—This method of cooling is simple and is most widely used. After induction of anæsthesia the subject is immersed in a cold bath, exposed to a draught of cold air, or surrounded by a cooling-blanket or ice-bags. The method has one disadvantage in that it has to overcome the vigorous reaction of the skin.

2. Blood Cooling.—This is more rapid than surface cooling. It is achieved by creating an artificial arteriovenous fistula with the aid of a long polythene tube. The blood is then cooled while it passes through the extracorporeal circuit. The method has the disadvantage that a major artery is used and possibly sacrificed, and therefore Ross (1954) has modified it by introducing a pump into the circuit which shunts the blood from a vein to a vein.

3. Body Cavity Cooling.—This is done by the introduction of a cooling-coil or cold saline into one of the body cavities, e.g., the pleural cavity. Khalil and MacKeith (1954) have suggested a method whereby cold water is passed through a balloon placed in the stomach of the subject.

Apparatus for Inducing Hypothermia by Intragastric Cooling.—

Description (*Fig.* 364).—The apparatus consists essentially of a refrigerating machine for cooling water circulated through a latex bag in the stomach of the patient. The unit of an ordinary household refrigerator has been used for this purpose and the evaporator or cooling-coil placed in a double-wall galvanized iron tank. Glasswool placed in the outer walls of this tank provides the necessary insulation and water is placed in the inner tank of 3–4 gallon capacity. An electrically driven centrifugal pump with an output range of ½–4 gals. per minute draws the cooled water from the inner tank and delivers it by means of one lumen of a double lumen tube to the latex bag. The water is returned from the bag through the other lumen back into the tank by syphon action. The apparatus is mounted on a suitable stand provided with wheels to facilitate easy transport.

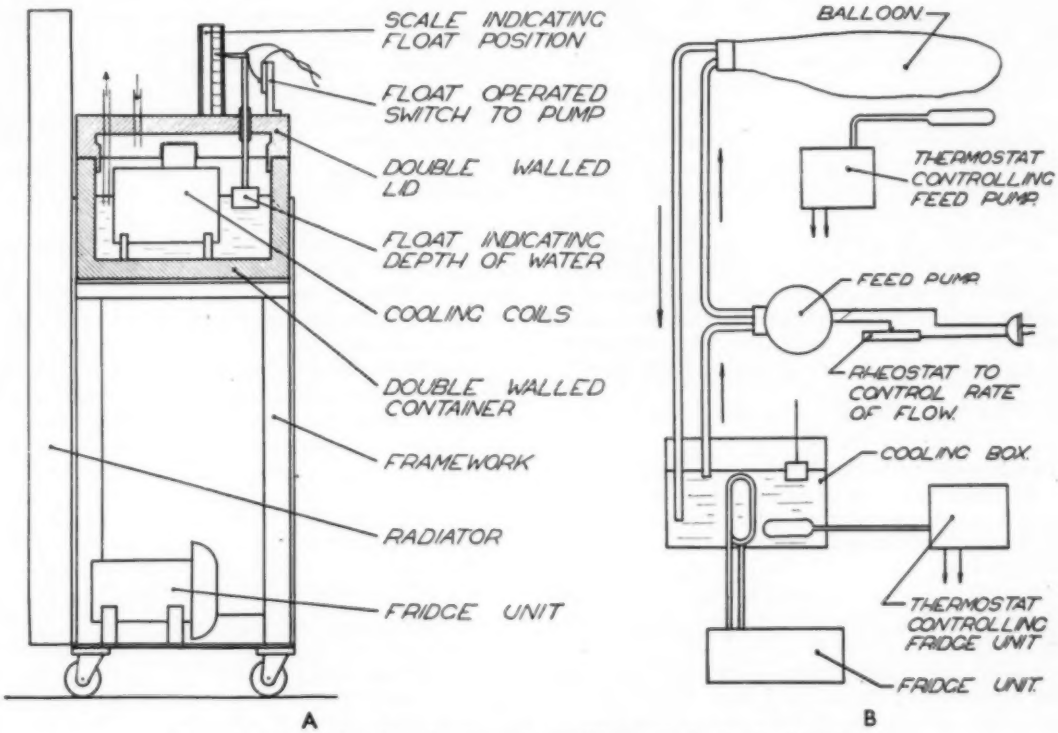

FIG. 364.—A, Section through apparatus; B, Diagrammatic circuit of apparatus.

Method of Operation.—The circulating water is cooled to a temperature just above freezing-point. This is achieved by controlling the refrigerating unit by means of a thermostat. The bulb of the thermostat is placed in the tank and set to arrest the mechanism when the water reaches a temperature of 5° C. and to start it again at 8° C.

The temperature of the patient is controlled by a second thermostat which starts or stops the circulating pump. The bulb of this thermostat is inserted into the rectum of the patient. The speed and hence the output of the pump is controlled by means of a rheostat.

The quantity of the cooling agent in the circulating tank is shown by means of a level indicator. This level can be kept at a desired point by means of a micro-switch operating from the level indicator which stops and starts the circulating pump.

The experiment is started by switching on the refrigerating unit which then rapidly cools the water in the inner tank. The volume to which the latex bag must be distended depends on the size of the patient's stomach. Before placing the bag in the patient's stomach it is filled with the desired volume of cooling agent and the drop in the level of the tank is noted. The micro-switch is then set to this level which ensures that the bag cannot be over-inflated and that the circulation of water will not continue should the bag rupture accidentally. (The circulating pump will switch off as soon as the pre-determined level is reached.)

Now the circulating pump is stopped and the latex bag is emptied and passed into the patient's stomach. Circulation is started and the bag distended to the desired volume. By adjusting the inflow by means of the rheostat and the return by means of the height of the bag above the lower end of the inflow, the bag can be kept distended whilst cold water circulates through it. Over-inflation of the bag to bursting point is prevented by the micro-switch.

As the temperature of the patient drops the respiratory movements become slower and shallower, and spontaneous breathing will eventually cease. Before this occurs, an intratracheal tube is passed

and the patient is hyperventilated to prevent CO_2 accumulation.

With intragastric cooling the body temperature of a patient can be lowered from 37° C. to 28° C. in 1½–2 hr. The preliminary stages of this cooling can be speeded up by applying surface cooling.

The possible risk of damage to the stomach by contact with the latex bag containing such cold fluid has been kept in mind. So far the method has been applied to 22 dogs and to 1 human patient. Careful clinical observations on the patient, who survived, and post-mortem examinations (including histological studies of the stomachs) on those dogs that succumbed during the operation, or were sacrificed afterwards, revealed no damage to the gastric mucosa or stomach wall.

Advantages.—The main advantages of this method of cooling are :—

1. The apparatus is relatively cheap, of straightforward design and readily transported.

2. It is possible to cool the patient on the operation table without any hindrance to the surgeon.

3. The method of applying the cooling procedure to the patient requires no major surgical procedure.

4. On completion of the surgical manœuvre for which hypothermia was applied, the patient can be brought back gradually to normal temperature by using the same apparatus but circulating heated water.

THE PLACE OF HYPOTHERMIA IN SURGERY

The serious complications that may occur in man by the artificial reduction in body temperature have at present limited the use of hypothermia only to surgical interventions where it is necessary to interrupt the blood-supply to vital organs. In the present state of our knowledge it is generally agreed that temperatures below 28° C. are dangerous. At this temperature it is possible :—

1. To occlude the venous return to the heart and work inside the heart chambers under direct vision. Unfortunately, ventricular fibrillation may occur at the end of 7–8 minutes unless blood is allowed back into the heart. Although hypothermia offers more time for working within the heart chambers under direct vision, the period available to the surgeon at 28° C. is too short to perform any major reconstructive surgery, e.g., the surgical treatment of mitral incompetence.

2. The blood-supply to the brain can be completely occluded with safety for a longer period of time than at normal temperatures. This places a valuable tool in the hands of the neurosurgeon, and if procedures could be rendered sufficiently safe the fields of aneurysmal surgery and other vascular neurosurgery could be extended. Lougheed and Kahn (1955) showed that in dogs at 25° C. the cerebral metabolic rate varied from 23 per cent to 35 per cent of normal. Of 8 dogs cooled to this temperature every one survived after having been ventilated with 100 per cent of nitrogen for 15 minutes. Only one showed neurological changes. Lougheed, Sweet, White, and Brewster (1955) report on a patient successfully operated on for an arteriovenous malformation of the brain under hypothermia. In this patient the cerebral circulation was arrested for as long as 14 min. 25 sec. at a time. The sum total period of occlusion of both carotids and both vertebral arteries was 47 min. 15 sec.

3. Lastly, in vascular surgery it is possible to clamp the aorta. Parkins, Ben, and Vars (1955) compared the end results in hypothermic and normothermic dogs when the aorta was occluded at the level of the eighth dorsal vertebra for periods of 30 min. to 2 hr. The survival rate was significantly higher and the complications much less in the hypothermic group.

I am indebted to Prof. J. H. Louw in whose Department this work was done for his constant help, criticism, and encouragement, and to Prof. R. H. Goetz for his co-operation and guidance. My thanks are also due to the Theatre Staff at the Groote Schuur Hospital, and the staff of the Animal House at the University of Cape Town Medical School. The refrigeration unit was kindly lent to us by Alberton Distributors (Pty.) Ltd.

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PANCREATICODUODENECTOMY AND PANCREATICOGASTROSTOMY

A FIVE-YEAR SURVIVAL, WITH NOTES ON THE METABOLISM

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Partial pancreaticoduodenectomy is an operation associated with a variable but usually high mortality and a considerable morbidity. Though radical excisions were carried out before (Codivilla, quoted by Sauvé, 1908; Kausch, 1912; and Hirschel, 1914), it was not till the publication of Whipple, Parsons, and Mullins (1935) that radical pancreaticoduodenectomy became a more or less standardized procedure practised by many surgeons. Though details differ, the two controversial points still outstanding are whether to do the operation in one or two stages, and how to deal with the tail of the pancreas left at the end of the operation and the source of much of the morbidity associated with it.

Ligature of the duct and cut end of the pancreas has many advocates and was the method originally tried. Brunschwig (1943), amongst others, advocates it and says there is no associated metabolic disturbance as a result. Cliffton (1952), in reporting 12 resections where the pancreas was not implanted, found fistula a real problem in only 1 case and 1 patient had uncontrollable metabolic disturbance. Cattell's (1949) first case in which the pancreas was ligated developed a fistula, and since then he has advocated pancreaticojejunostomy, for this reason and to preserve the external pancreatic secretion to the body economy. Miller, Dockerty, Wollaeger, and Waugh (1951), in reporting a series of cases, had 50 per cent pancreatic fistulæ following ligation and 12·5 per cent following pancreaticojejunostomy. The third method of dealing with the pancreas was suggested by Wells and Annis (1949) in experimental work on the dog. This was similar in some respects to that previously published by Tripodi and Sherwin (1934) and Person and Glenn (1939). Because it was thought that the intestinal juices would activate trypsinogen and so interfere with the anastomosis between pancreas and jejunum, the stump of the pancreas was anastomosed to the stomach. Wells notes that his first two cases in which the pancreas was ligated were not followed by fistulæ, whereas the next two in which the pancreatic stump was anastomosed to the jejunum were complicated by fistula formation. Reports of the success of pancreaticogastrostomy in the human patient have been published (Wells, Shepherd, and Gibbon, 1952; Dill-Russell, 1952; and Nanson, 1954), and the efficacy of the secretion going into the stomach has been demonstrated post-operatively by Ingebrigtsen and Langfeldt (1954) and by Nanson (1952). The survival rate is low, and Muir (1955) has recently reviewed this and commented on it. He rightly points out that it is not much inferior to that obtained as a result of surgery in cancers of the foregut generally. Because of the relatively few pancreaticogastrostomies performed, and because of the poor survival rate, it was thought of interest to put on record the late result of one such resection and anastomosis.

CASE REPORT

Mrs. H., aged 69, was referred to the General Hospital, Birkenhead, by Dr. I. Harris, being admitted on Nov. 19, 1949. She gave a history of an attack of painless jaundice lasting about eight weeks and which started eight months previously. This was said to have cleared, but eight weeks before admission it reappeared. It varied in intensity and she thought it was clearing. There had been no pain or vomiting, but she had had nausea and a distaste for fats. Her bowels were stubborn and pale and she had noted her urine to be dark. She had acid regurgitation and considerable flatulence which she brought up. There were no relevant past illnesses.

On Examination.—She was a deeply jaundiced elderly woman with a firm palpable liver. Rectal examination was negative. Blood-pressure was 165/95 and there was a doubtful systolic murmur at the apex. There were no obvious abnormalities in the other systems. Her urine contained pus cells and bile. Liver function tests on Nov. 19 were: van den Bergh positive direct; Serum-bilirubin 25·6 mg.; Serum alkaline phosphatase 27 units per 100 c.c.; Total protein 5·82 g. per cent; Serum-albumin 2·66 and Serum-globulin 3·16 g. per cent; Colloidal gold 100,000; Cephalin cholesterol +; Thymol turbidity 5 units; Prothrombin time 17 sec. Serum-bilirubin on Nov. 24 was 15 mg. per cent. A blood-count showed 4,400,000 R.B.C. with 75 per cent hæmoglobin; leucocytes in normal proportions totalled 6400. The blood-urea was 20 mg. per cent.

At Operation (Nov. 26).—Through a Kocher incision, a mass taken to be a carcinoma was found involving the head of the pancreas. Stones were present in the gall-bladder. The head of the pancreas and the duodenum were mobilized, and the head and neck of the pancreas and the first and second parts of the duodenum, with the pyloric end of the stomach, were resected. The duodenum at the junction of the second and third parts was invaginated and closed. The stump of the pancreas with its duct was drawn into an opening made in the back of the stomach by sutures which were brought from within out and stitched to the outer aspect. The opening in the posterior wall of the stomach was snugly attached to the adventitia of the pancreas by a few interrupted sutures. The stones were removed from the gall-bladder and the opening closed. A loop of jejunum about a foot from the duodenojejunal flexure was brought behind the colon, the common bile-duct anastomosed to the apex and the cut end of the stomach to the efferent loop below it. The hole in the mesocolon was closed snugly around the loops of the small intestine. The wound was closed with drainage at the outer end of the incision.

The immediate post-operative period was associated with oliguria and drowsiness; she passed 2 oz. of urine in the first 24 hours and 8 oz. in the second. Her blood-urea rose to 61 mg. per cent. A pint of sodium sulphate solution was given on the second day; she had been on continuous intravenous therapy since operation, and she improved.

On Dec. 8 her blood-urea was 22 mg. per cent and the serum-bilirubin 2·3 mg. per cent. Examination of her fæces on Dec. 10 showed a formed stool normally pigmented, with muscle-fibres normally digested and not in excess and with no excess fats. The pathological report on the tumour was adenocarcinoma of the duodenum infiltrating the head of the pancreas. She was discharged from hospital on Dec. 13.

She continued well until July 25, 1954, when she was admitted to Clatterbridge Hospital. On the morning of admission she had had a bout of vomiting, bringing up bile, and this was followed by epigastric pain which was dull and continuous. Her bowels had been moved the day before. Examination revealed an obese lady with tenderness in the epigastrium and right hypochondrium and a sense of resistance. Her blood-pressure was 250/130, pulse 80, and temperature 98·2. The diagnosis

FIG. 365.—Barium meal demonstrating the biliary system.

was in doubt and the possibility of a stomal ulcer perforation or biliary infection was considered. Serum-bilirubin was 2·6 mg. per cent and serum-amylase 50 units per 100 ml. A radiograph of her abdomen showed no distension and no free gas under the diaphragm. Her white-cell count was 12,600. On July 28, when I first saw her, there was a swelling in the right hypochondrium which I thought was her gall-bladder. Her temperature rose and she was given aureomycin for ten days. The temperature continued to fluctuate, but the abdominal signs abated and though she looked ill the old lady insisted she was better. Liver function tests on Aug. 7 showed: Serum-bilirubin 1·3 mg. per cent; Total protein 6·3 g. per cent; Serum alkaline phosphatase 15 units per 100 ml.; Thymol turbidity 2 units. Her temperature subsided and a radiograph of her gastro-intestinal tract on Aug. 11 showed no evidence of any ulceration, but the meal outlined the biliary channels (*Fig.* 365). No pancreatic duct was apparent. Her blood-sugar on Aug. 18 was 86 mg. per cent. Her temperature started to rise again on Aug. 21 and she was given penicillin injections. Blood-culture on Aug. 23 was negative and her urine contained only a few pus cells. Examination of the fæcal fat showed total fat 20·4 g. per cent of dried fæces, with 19·9 g. per cent split fat and 0·5 g. per cent unsplit. She continued pyrexial and was given terramycin. Her temperature subsided, only to rise again, and on Sept. 10 she started a second course of terramycin. During her apyrexial period aspiration of her stomach contents on Sept. 8 was tested for trypsin by Spencer's (1947) method and it was found to show a trypsin activity more than six times that of normal gastric juice. Her general condition continued to deteriorate, and she developed diarrhœa, her blood-pressure being 140/80. An ill-defined swelling was noted in the right hypochondrium and this burst on Oct. 10. Culture of the pus showed *B. coli* and atypical *B. coli* sensitive to chloromycetin in the main, and a course of this was started some days later. Liver function tests about this time showed total protein 5·1 g. per cent, bilirubin content 0·6 mg. per cent, alkaline phosphatase 16 units per 100 ml., and thymol turbidity negative. The sinus continued to discharge and a lipiodol radiograph on Oct. 18 showed a track an inch long and with no demonstrable communication with any intra-abdominal structure. She was anxious to go home and she was allowed to do so on Nov. 10 with the sinus still discharging. A further attempt to outline the sinus failed, but a translucency was noted in the area which was thought to be in the chest. Further radiographs of this on June 16 showed this to be a cyst in the posterior basal segment of the right lower lobe (a bronchial cyst) with no evidence of a dissociated segment of lung. There was general cardiac enlargement (Dr. Keating). At this time she was well in herself but with some constipation. She was last seen on July 14 when her sinus had healed and she was very well.

DISCUSSION

This patient, both clinically and biochemically, has suffered no loss in the efficiency of her gastro-intestinal tract as a result of her pancreaticogastrostomy and resection. At no time has she suffered from diarrhœa or bulky or fatty stools, she has not lost weight, and examination of her gastric juice would seem to show that her pancreas is functioning and its external secretion is being secreted into her stomach and utilized. It must be conceded nevertheless that patients who have had their ducts ligated do not all suffer from pancreatic insufficiency nor are patients who have had their pancreatic ducts implanted into the jejunum necessarily free from such deficiencies. Wollaeger, Comfort, Clagett, and Osterberg (1948), in investigating this problem, reported a series of 10 cases, 3 of whom had ligation of the duct, 1 interestingly had a pancreaticogastrostomy and partial pancreatectomy but for advanced chronic pancreatitis, and 6 had pancreaticojejunostomy. They found evidence of marked deficiency in the utilization of fats and proteins as noted from examination of the dried fæces in the patients in whom the duct was ligated and in the patient with a pancreaticogastrostomy. The result in the latter case was attributed by them to the existing marked destruction of the remnant of pancreas anastomosed. In these patients utilization was much improved by the exhibition of 15 pancreatin tablets of 5 gr. (0·3 g.) daily, the loss of fat in the fæces being cut by 44·6 per cent and that of protein by 53·4 per cent. In the cases treated by pancreaticojejunostomy, the utilization varied from that seen in the previous cases to a loss just above normal. This difference may be due partly to the efficiency of the remaining pancreatic tissue and partly to the effectiveness of the anastomosis. It must be borne in mind that after a partial gastrectomy in patients with a presumably normal pancreas there is a variable excess loss of fæcal fat, and this factor, whatever may be its cause, may be

an additional reason for the differences found after partial pancreatectomy. In contrast to these findings, Whipple and Bauman (1941) had 2 of 4 patients and Brunschwig and Allen (1943) had 1 of 3 patients in whom the duct had been ligated and who had normal fæcal loss of fat and protein. Wollaeger and others (1948) suggest that this may have been due to the development of a spontaneous post-operative fistula between the ligated pancreas and the gastro-intestinal tract. The possibility of the existence of functioning pancreatic rests in the intestinal tract should perhaps also be considered in these cases. It might be thought that investigation of patients who had undergone total pancreatectomy would shed some light on the importance of the pancreas. There is increased loss of fæcal protein and fat, but the latter is not necessarily associated with clinical diarrhœa. Priestley, Comfort, and Radcliffe (1944) in a patient who had a total pancreatectomy for an islet-cell adenoma found fæcal fat to consist of 37 per cent of fæcal solids on a fat intake of 69 g. corresponding to a loss of 70 per cent of the ingested fat, 43 per cent on a fat intake of 102·5 g. with a loss of 35 per cent of the ingested fat, and 54 per cent on a fat intake of 95 g. together with 28 g. daily of gelatin-coated capsules of powdered pancreatin (Parke, Davis & Co.) equivalent to a loss of 42 per cent of the ingested fat. The pancreatin had to be discontinued in this case after five days because of the patient's refusal to continue to take it. Of the fæcal fat, 54–69 per cent was neutral fat. The daily loss of fæcal protein varied between 25 and 39 per cent of the fæcal solids, that is a loss of 25–55 per cent of the ingested protein. The amount of protein excreted in the fæces was less when the patient was receiving pancreatin, but the fæcal fat loss was not significantly altered. Whitfield, Gourevitch, and Thomas (1952), in reporting a patient who had had a total pancreatectomy for a duct papilloma which had produced obstruction with stasis and such induration as to simulate a carcinoma, found on a diet which included 75 g. of fat daily together with 1·5 g. of pancreatin that the fæcal fat was 62 per cent of the intake, while when 11·5 g. of pancreatin was given daily the loss was only 17 per cent of the intake. Fatty acids were 73 per cent of total fæcal fat. The fæcal protein loss varied between 30 and 43 per cent of the intake and was not affected by the ingestion of pancreatin. The effects of pancreatin in this patient were the reverse of those found in the patient reported by Priestley and others (1944). In this patient there was no clinical diarrhœa, the patient had three bulky ill-formed stools which with pancreatin became less bulky and of more normal consistence but were not less frequent. In a personal case where total pancreatectomy was performed for carcinoma of the pancreas which microscopically was found to have involved the whole gland, fæcal fat was 46·16 per cent of dried fæces, of which 86·3 per cent was split fat. The fæcal loss was 79·2 per cent of the intake, which was 90 g. a day, the investigation being conducted over 72 hours. The amount of moist fæces passed during the three days was 1507·31 g. On a total nitrogen dietary intake of 15 g., fæcal nitrogen was 7·4 g. and urinary nitrogen 6·5 g.—that is, the fæcal nitrogen excretion was 52·6 per cent of the intake and the urinary nitrogen excretion 43·3 per cent, against average normal findings of fæcal loss of 8·9 per cent of the intake and urinary nitrogen excretion of 83 per cent (Dr. H. MacLean). This patient died nine months after the operation from metastases.

These cases all demonstrate that the loss of external pancreatic secretion is associated with gross defects of fat absorption and also in defects of protein digestion and absorption. It would seem advisable, therefore, in patients who undergo partial pancreatectomy, to utilize the external pancreatic secretion by anastomosing the duct to the gastro-intestinal tract. The differences that are found between individual patients subjected either to ligation of the duct or anastomosis depend on: (*a*) The efficiency of the pancreatic remnant; (*b*) The possible development of spontaneous internal fistulæ in the former or fibrosis of the anastomosis in the latter; (*c*) The individual variation in the effect on fat metabolism of the partial gastrectomy itself; and (*d*) The possible existence of pancreatic rests.

Investigation of the metabolism of patients who have undergone pancreaticogastrostomy and partial pancreatectomy have been few, but the findings of Ingebrigtsen and Langfeldt (1952), Nanson (1954), and this case make it evident that following the operation not only is pancreatic juice secreted into the stomach in the immediate post-operative period, but continues to be secreted for many years with beneficial effect on the processes of digestion.

In the management of patients who have undergone pancreatic resection and in whom the efficiency of digestion is impaired, it has been found that with extra fat and protein in the diet, though there was greater loss of fat and a slightly greater loss of protein in the fæces, there was greater absorption of both. Because of subjective symptoms, however, it was suggested that the diet should contain 50–75 g. of fat, 120–140 g. of protein, and plenty of carbohydrate supplemented by 15 g. daily of enteric-coated capsules of pancreatin. The latter, however, may not be well tolerated, and Nardi (1952) describes a patient after total pancreatectomy whose appetite and caloric intake were improved after the discontinuance of the pancreatin. This patient found that the untoward gastric symptoms which he had while taking the pancreatin were not offset by the slight improvement in the consistency and frequency of the stools and he refused to take it. In some patients, therefore, the deterioration of the appetite may offset the benefits of pancreatin and the total caloric intake suffer as a consequence.

SUMMARY

1. A patient with a peri-ampullary carcinoma arising in the duodenum and invading the pancreas and surviving six years is reported.

2. The patient, who had a pancreaticogastrostomy and partial pancreaticoduodenectomy, suffered no loss of efficiency of her digestive system.

3. The presence of trypsin in the gastric juice six times the normal quantity was found to be present five years after the operation.

4. The metabolic changes following pancreatic resection are noted.

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ABDOMINAL PERIARTERITIS NODOSA

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THE diagnosis of periarteritis nodosa has always been somewhat difficult, and even at the present time the condition may be revealed first at autopsy. On occasion it presents itself as an abdominal condition requiring surgical consideration, and Jernstrom and Stasney (1952) have referred to a 'diagnostic dilemma' in such a case.

This paper describes 3 cases of periarteritis nodosa which were of surgical importance. Attention is paid to their clinical aspects in conjunction with the pathological findings, and an attempt is made to clarify the 'dilemma'.

CASE REPORTS

Case 1.—E. L., a female aged 68 years, who presented in December, 1946, with a six-year history of gastric ulceration. This was confirmed at operation when a partial gastrectomy was performed. The histology of the resected stomach revealed chronic peptic ulcer in active phase.

The subsequent history was uneventful until January, 1951, when an acute febrile illness occurred, characterized by cough, hæmoptysis, and dyspnœa. These symptoms diminished in severity but asthma persisted and anorexia, constipation, and loss of weight were noted. Readmission occurred in April, 1951, after a further hæmoptysis.

ON EXAMINATION.—Pallor, dyspnœa, and loss of weight were evident and chest examination suggested a diffuse bronchopneumonia, confirmed radiologically. The urine contained albumin, pus cells, and casts. The patient had a post-gastrectomy macrocytic hyperchromic anæmia which did not respond to vitamin B_{12} therapy. The E.S.R. was 55 mm./1 hr. (Westergren).

While in hospital paroxysmal attacks of tachycardia associated with congestive heart failure were observed and death occurred in syncope.

AT AUTOPSY.—The body of a frail elderly woman weighing 34 kg., with striking pallor of skin and mucous membranes. A healed abdominal surgical scar was present. Fresh blood and blood-clot filled the abdominal cavity. Inconspicuous beaded thickenings were found along branches of the superior mesenteric artery. One of these thickenings was a small aneurysm which had ruptured. The heart was not enlarged, the myocardium was soft, and the wall of the coronary arteries was thickened in places. Bilateral serous pleural effusions with numerous stringlike fibrous adhesions were present on the left side. These were related to scattered areas of chronic pneumonitis in the left lung. Other abnormalities included a small nodular colloid goitre, a solitary cholesterol gall-stone, and partial gastrectomy had been performed.

HISTOLOGY.—Periarteritis nodosa was found, affecting the kidneys, lungs, heart, and mesenteric arteries. The mesenteric vessels affected were branches of the superior mesenteric artery of a size range 0·1–0·3 cm. One vessel contained recent thrombus. Another showed segmental destruction and replacement by granulation tissue which had subsequently stretched and given rise to a small aneurysm (*Fig.* 366). The arteries are cuffed with leucocytes.

Comment.—Massive spontaneous intraperitoneal hæmorrhage has been recorded and the literature surveyed (Brewer and Marcus, 1948), but the association with periarteritis nodosa has not received especial mention. This case, which has similar clinical features, was due to a ruptured aneurysm of a branch of the superior mesenteric artery. Further healed lesions of periarteritis nodosa were found in the mesenteric, coronary, renal, and pulmonary arteries. Symptoms were present for five months before death, and these were confined chiefly to the respiratory system.

It is recognized that mucosal ulceration in the gastrointestinal tract may be caused by occlusion of arterial vessels in the submucosa brought about by periarteritis nodosa (*see Case* 2). The sections of the gastric ulcer removed in 1947 were re-examined with this in mind, but there was no evidence in favour of this aetiology. The vessels in the wall of the ulcer showed endarteritis such as is commonly seen in peptic ulceration.

Case 2.—H. H. B., a male aged 35 years, was admitted to hospital on three occasions, February, August, and December, 1952.

On the first occasion he gave a six-months' history of cough productive of purulent sputum associated with breathlessness. The condition resolved satisfactorily on penicillin therapy within a few days.

On the second occasion the symptoms had recurred and asthmatic attacks were a new feature. This illness rapidly responded to streptomycin therapy.

In December he complained of abdominal pain and vomiting of two weeks' duration. The pain was severe, felt around the umbilicus, and constant. Vomiting occurred daily. The epigastrium was tender to palpation. A further history of dyspeptic pain for many years and recent loss of weight was obtained.

Laboratory investigations revealed albuminuria, red and white cells and casts in the urine, and moderate leucocytosis with marked eosinophilia and a raised E.S.R.

Lumbar girdle-pains and left wrist-drop developed suddenly while in hospital.

A barium meal indicated a gastric ulcer and on Dec. 30 a partial gastrectomy was performed. (*Fig.* 367.)

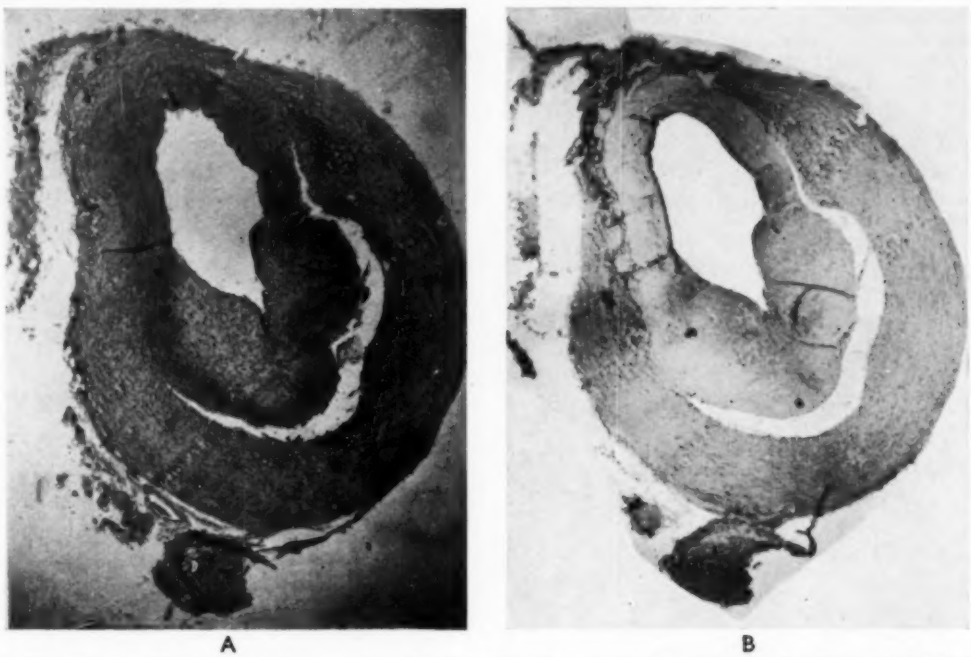
He survived only two months, during which time polyneuritis progressed to flaccid quadriplegia, despite ACTH therapy. Asthmatic attacks also recurred.

MORBID ANATOMY.—Operation specimen: stomach. The specimen consisted of part of the stomach with a cuff of duodenum. On the posterior wall of the pylorus there were grouped mucosal hæmorrhages covering an area of 2·5 cm. in diameter. There was no ulceration present.

Microscopically numerous arteries and arterioles in the stomach wall and mesentery showed the changes of acute and healing periarteritis nodosa. Many arteries showed segmental or complete fibrinoid necrosis, and contained organizing thrombus. There is intense cuffing of the damaged arteries with inflammatory cells, and chief among these is the eosinophil leucocyte. Arterioles are less severely damaged, but many are cuffed with leucocytes. Numerous small mucosal hæmorrhages and some microscopical erosions were also present. (*Fig.* 368.)

AT AUTOPSY (R. A. Cocks).—An emaciated adult male with healed upper right paramedian incision. The heart was normal in size and appearance. There was diffuse bronchopneumonia and fibrous pleural adhesions of the right lower lobe. Small mucosal hæmorrhages were seen in the mucosa of the gastric remnant and rectum. The kidneys showed no striking changes.

HISTOLOGY.—Acute lesions of periarteritis nodosa were found in the small intestine (*Fig.* 369), and healed



A B

FIG. 366.—*Case* 1. Transverse section of a branch of the superior mesenteric artery showing its segmental destruction. The lesion is in the healing stage and the new-formed fibrous tissue has stretched, causing a nodular swelling of the vessel wall. A, H. and E. (× 25); B, Sheridan's elastic (× 25)—shows the partial destruction of the internal elastic lamina.

FIG. 367.—*Case* 2. Radiograph of stomach after barium meal, showing deformity, elongation, and stenosis of the pyloric antrum.

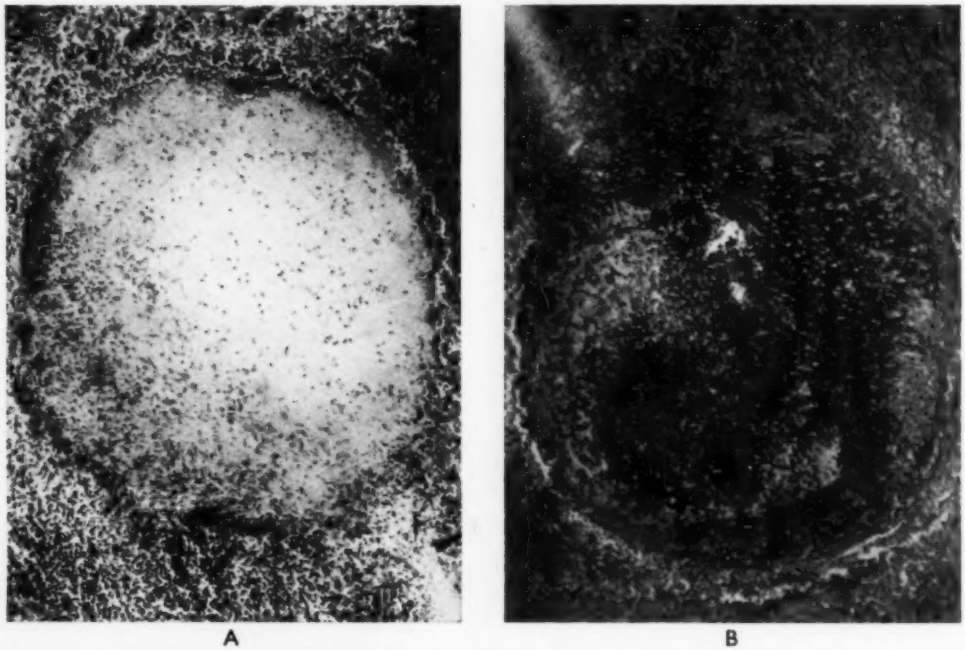
lesions in striped muscle taken from the upper arm. The kidneys were the seat of the microscopical type of periarteritis nodosa with severe and widespread glomerular damage described by Davson, Ball, and Platt (1948). Hypertensive vascular changes were not apparent.

Comment.—This man's disease was generalized and ran a stormy course lasting a year. The disease was still active in some arteries of the small intestine at death. Unlike the stomach these lesions were clinically silent. The kidneys were severely damaged and uræmia could not have been long delayed.

Case 3.—J. S., a male aged 64 years, was referred to hospital with suspected appendicitis.

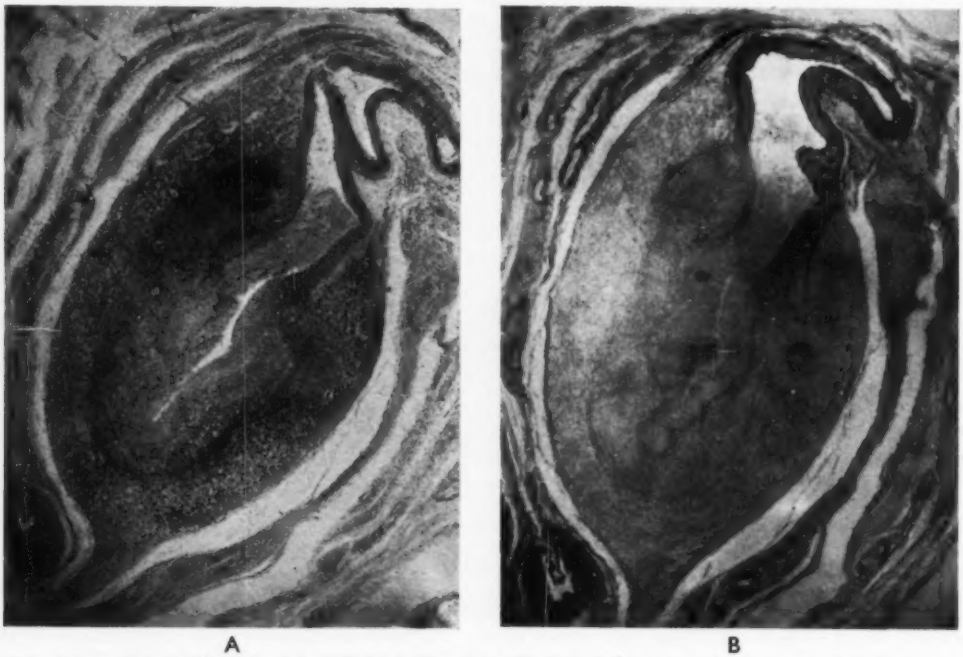
A week before admission he noticed pain in the epigastrium, which three days later moved to the right iliac fossa. He vomited all the day before admission, and the bowels were opened for the first time for days.

Eighteen months before admission he had had pain in the back and foot-drop, which cleared up spontaneously in a few weeks. Laparotomy was advised because on physical examination guarding and rigidity were present in the right iliac fossa.



A B

FIG. 368.—*Case* 2. Stomach, operation specimen, showing a small subserosal artery which is totally destroyed and replaced by thrombus. Very numerous granular leucocytes are present, which are mostly eosinophils. A, H. and E. (× 66·6); B, P.T.A.H. (× 66·6)—the fibrin content of the recently deposited thrombus is shown up more clearly.



A B

FIG. 369.—*Case* 2. Small intestine, post-mortem specimen, showing an artery of the subserosa cut lengthwise. A segment of its wall is necrotic and swollen by inflammatory exudate. A, H. and E. (× 25); B, Sheridan's elastic, showing destruction of internal elastic lamina (× 25).

Laparotomy (Dec. 16, 1954): the terminal ileum was found to be gangrenous and excised. The small intestine was anastomosed to the transverse colon. Arterial pulsation was absent in the mesentery serving the terminal ileum. The appendix was not removed.

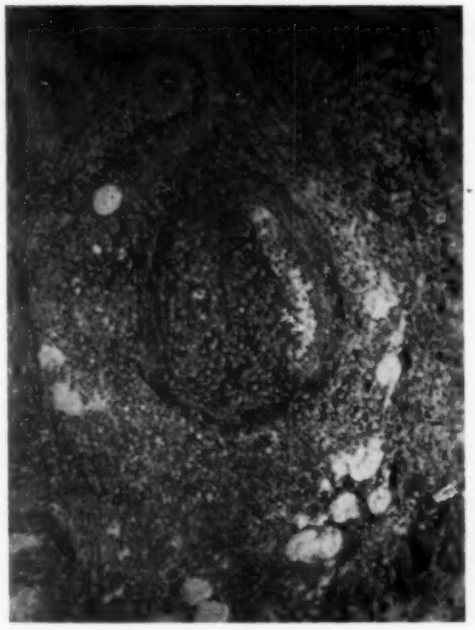
FIG. 370.—*Case* 3. Part of the resected terminal ileum opened lengthwise. The dark areas are infarcted and ulcerated. There is a healthy area on the right of the picture where the valves of Kerkring are preserved.

MORBID ANATOMY.—The specimen consisted of 23 cm. of small intestine with attached fatty mesentery. The intestine was plum-coloured, stiff to handle, and plaques of fibrin were present on the serosa. The gut wall was thickened and extensively ulcerated in a shallow and irregular manner without regard to Peyer's patches. The floor of the ulcers was necrotic and red, and the surrounding mucosa hæmorrhagic. The mucosa between the ulcers was in places entirely normal. (*Figs.* 370, 371.)

Histologically, there was typical acute periarteritis nodosa indiscriminately affecting the submucous arterial plexus of a size range 350-100 μ. Circulatory arrest in some vessels due to secondary thrombosis had produced ischæmic necrosis of the overlying mucosa which had sloughed to produce shallow ulcers. The mesenteric vessels were normal.

PROGRESS.—The histological findings prompted a thorough investigation to find evidence of a generalized arteritis. No stigmata of the disease could be found clinically or after laboratory investigation of urine, blood-cell counts, or serum-proteins, but eight days after the operation there was evidence of peripheral neuritis with right foot-drop. Cortisone was presented and the patient made a complete recovery and remains well without therapy.

A



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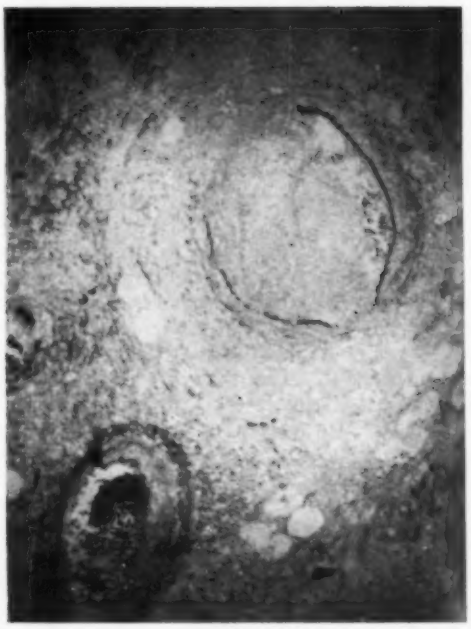

C

FIG. 371.—*Case* 3. Periarteritis, acute, in an artery of the submucous plexus of the terminal ileum. Vessel wall largely destroyed and lumen full of fresh thrombus. The inflammatory cells infiltrating the vessel wall and perivascular tissues are mostly polymorphonuclear leucocytes. A, H. and E. (× 80); B, P.T.A.H. (× 80)—shows fibrin threads in thrombus and necrotic arterial wall; C, Sheridan's elastic (× 80)—the interruption of the internal elastic lamina is evident.

Comment.—Although exhaustive investigation failed to reveal further evidence of the disease in a more generalized form, it was proposed to guard against its presence by the administration of cortisone. When foot-drop, peripheral neuropathy (Heathfield and Williams, 1954) occurred eight days after operation there was clinical confirmation of the microscopical findings.

DISCUSSION

Pathology.—Since the classical description of periarteritis nodosa by Kussmaul and Maier (1866) and the first account in English by W. E. C. Dickson (1908), many reviews of large numbers of cases have appeared (Harris, Lynch, and O'Hare, 1939; Boyd, 1938; Miller and Daley, 1946). The majority of writers consider that the condition represents a vascular reaction of allergic nature (Rich, 1942, 1945; Rich and Gregory, 1943; Harris and others, 1939; Wilson and Alexander, 1945) and that a variety of initiating factors may be responsible, especially serum or sulphonamides. The older theories of a specific streptococcal infection (Vining, 1938) or a virus hypothesis (Harris and Friedrichs, 1922) have been discarded. It has also been considered as a manifestation of the adaptation syndrome (Selye and Pentz, 1943).

The morbid anatomical appearances are well known and have been restated by Harrison (1953).

Briefly, the disease may affect any artery or arteries in a random fashion, but shows a predilection for small muscular arteries or arterioles of the thoracic or abdominal viscera. Nodular swellings along the course of an artery are characteristic, but these are sometimes inconspicuous and often absent.

The histological findings are characteristic and may allow a positive diagnosis in biopsy material when subcutaneous or intramuscular vessels are involved, or in resected specimens referred for routine examination.

In the acute stage there is a focal periarteritis with fibrinoid necrosis of the arterial wall. The lesion may involve the whole circumference of the vessel or only a segment. Elastic is destroyed and the vessel is cuffed with granular leucocytes and monocytes which extend into the necrotic zones.

Sequelæ.—Circulatory arrest with consequent infarction may occur when there is superadded thrombosis or occlusion through intimal proliferation (*Case* 3). Aneurysmal dilatation may occur after segmental destruction of the artery wall, introducing the risk of rupture with hæmorrhage which may prove fatal (*Case* 1). Healing occurs spontaneously as is shown by histological examination. In these cases arteries may have been turned into fibrous cords in which a few leucocytes linger.

Cortisone suppresses the inflammatory features of the disease and may serve to prevent functional destruction of arteries supplying vital organs (*Lancet*, 1954).

Clinical Features (General).—

Age.—The disease may affect persons of any age or either sex, but is said to be commonest in males in the fourth decade (Harrison, 1953).

Course.—The disease may run a short, stormy course with a fatal outcome in a matter of weeks. More usually, however, the clinical pattern is one of a prolonged illness. Although Fishberg (1923) suggested that the duration of disease is from three to six months, it is now recognized that it may be protracted for years (*Case* 1); similarly, the earlier case fatality reports of 100 per cent (Klotz, 1917) and Harris and others (1939) 90 per cent are considered excessive, in view of the many records of recovery (Heathfield and Williams, (*Case* 8), 1954; our *Case* 3; Klein, 1949; Spiegel, 1936).

The clinical picture is that of a non-specific subacute or chronic pyrexial wasting illness with tachycardia disproportionate to the severity of the fever (Davson and others, 1948). Loss of weight, asthenia, and malaise are common symptoms; irregular fever, tachycardia, raised E.S.R., granulocytic leucocytosis of neutrophil or eosinophil series and microcytic hypochromic anæmia are common signs.

The frequency of manifestations referable to certain organs may be compared to the frequency that internal organs are found to be affected in necropsy studies (Harris and others, 1939). Thus the kidneys are involved in 87 per cent, giving a nephritic or a hypertensive picture, and the heart in 84 per cent, producing either myocardial infarction or chronic ischæmic cardiac failure.

The lungs are involved in 25 per cent of cases and give rise to asthmatic, bronchitic, pneumonic, or phthisical clinical pictures.

Cutaneous involvement is present in 30 per cent of cases and leads to a variety of lesions, including nodular swellings, hæmorrhages, and ulceration (*Lancet*, 1955).

Involvement of peripheral nerves gives rise to combination of polyneuritic or polymyositic features.

Intra-abdominal Lesions and their Clinical Manifestations.—The abdominal manifestations of the disease occur in 50 per cent of cases (Arkin, 1930) and are so varied that it is proposed to enumerate certain clinical pictures that may be simulated :—

Peptic Ulceration.—When small arteries or arterioles within the stomach wall are affected, the mucosa may become ischæmic and suffer ulceration. This gives rise to dyspeptic pain, hæmatemesis, or melæna; or, in a later stage, fibrosis may lead to obstructive symptoms as in *Case* 2.

Such ulcers may perforate (Allen, 1940; Miller and Nelson, 1945) and fatal peritonitis with subphrenic abscess may result (Spiegel, 1936). Periarteritis nodosa as the cause of such ulceration is suggested by the site and distribution of the gastric lesion, and support of the diagnosis is lent by the associated symptomatology and history.

Intestinal Vascular Occlusion.—The mesenteric arteries may be affected by occlusive disease producing the picture of acute mesenteric thrombosis with infarction of loops of small intestine, according to the site, although Johnson and Baggenstoss (1949 a, b) in discussing mesenteric vascular occlusion, found only 3 cases due to periarteritis nodosa out of 60 cases of classical mesenteric thrombosis. Melæna may result (Wold, 1949) or necrosis of the bowel wall, leading to perforation and peritonitis (Logue and Mullins, 1946; Spiegel, 1936). Involvement of the smaller vessels results in discrete infarction of the bowel wall, more obvious in the small intestine, e.g., *Case* 3. Diagnosis before this, as in Manges and Baehr's (1921) case, where the surgeon (Buerger) recognized the condition, is exceptional.

Successful cases of resection are infrequent (Miller and Daley, 1946), and the prognosis is doubtful (Berris, Sawyer, and Lubchenko, 1948). Occasional ulceration without perforation may produce a sprue-like syndrome (de Navasquez and French, 1947). The diagnosis before operation may be confused with appendicitis, as in our *Case* 3. Appendicitis due to periarteritis nodosa may occur, however (Benedict, 1907; Lamb, 1914; Plaut, 1931; Friedberg and Gross, 1934; Druss and Maybaum, 1934); and Spiegel (1936) performed 4 appendicectomies in his series of 17 cases with good results.

Changes in the large gut may give rise to typical ulceration, which may be viewed on sigmoidoscopy (Mondor, Ducroquet, and Olivier, 1939; Felsen, 1941). The appearances described were those of horizontal linear streaking with localized vascular dilatations. In all cases the diagnosis may be difficult until microscopical examination of the tissues removed has been effected.

Intra-abdominal Hæmorrhage.—Hæmorrhages may occur either extraperitoneally or into the peritoneal sac. In *Case* 1 a fatal hæmorrhage occurred spontaneously from a small aneurysm along a tributary of the superior mesenteric artery.

Retroperitoneal hæmatoma may simulate a malignant tumour or appendicitis (Balo and Nachtnabel, 1929) or renal neoplasm (Miller and Daley, 1946).

Massive, spontaneous, intra-abdominal hæmorrhage has been recorded (Brewer and Marcus, 1948). West and Newnes (1953) describe a case of fatal hæmorrhage due to periarteritis nodosa whilst undergoing treatment with cortisone for rheumatoid arthritis. In such cases periarteritis nodosa as the possible cause obviously needs careful consideration, since a minute ruptured aneurysm may be extraordinarily difficult to demonstrate, as in *Case* 1.

Other Viscera.—Splenic infarction and enlargement (*Case* 2; Harris and Friedrichs, 1922) and pancreatic involvement (Miller and Daley, 1946) are described. In the latter a clinical picture varying from epigastric discomfort to catastrophic hæmorrhagic pancreatitis may occur. The classical paper of Davson and others (1948) surveys the association of periarteritis nodosa in the kidney with hypertension. Less commonly, hæmaturia simulating neoplasm (Powel and Pritchard, 1932), renal carbuncle (Keegan, 1925; Gray, 1932), and colic (Gray, 1932; Hauser, 1934) have been described.

Periarteritis nodosa may masquerade for a time as a primary disease of the liver (Mowrey and Lundberg, 1954), although lesions in the liver without impairment of function are more frequent, leading to aneurysm formation, infarction, and cirrhosis. Ulceration of the gall-bladder is described by Spalding (1940).

SUMMARY

Patients with periarteritis nodosa may be referred to the surgeon on account of abdominal lesions. These have been indicated and discussed with reference to three cases. The appreciation of the general condition of the patient is an important step in arriving at a diagnosis. Laparotomy may be life-saving in certain circumstances, and subsequent medical treatment may be of equal value.

Case 1 was under the care of Professor G. W. Pickering in St. Mary's Hospital, and the autopsy was performed under the supervision of Professor W. D. Newcomb.

Case 2 was admitted to the West Herts Hospital; the morbid anatomy was performed under the supervision of Dr. C. Pike, who has allowed us to examine all the available material.

Case 3 was admitted to the St. Albans City Hospital. This man remained well until June, 1956, when a further 37 cm. of small intestine was resected. The pathological changes present were similar to the original specimen.

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GASTRO-INTESTINAL SYMPTOMS IN POLYARTERITIS NODOSA

REPORT OF A CASE

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POLYARTERITIS nodosa was first described by Kussmaul and Maier in 1866. It is a disease characterized by multiple and focal degenerative lesions affecting mainly the smaller arteries and the vasa vasorum of the greater vessels. Consequent on these changes the affected vessels either become thrombosed or the wall is so weakened that aneurysms are formed. It is from the appearance produced by this latter occurrence that the disease derives its name.

Since the lesions are widely disseminated and result in ischæmia of the tissues supplied by the affected vessels, it is not surprising that the clinical features of the disease are inconstant and variable, depending on the diversity of the arterial involvement. It is because of these protean manifestations that the disease may be suspected on purely clinical grounds.

Abdominal pain is frequently present, but its significance is not always apparent. It may occur in the absence of any gross or easily detected intra-abdominal lesion, or may herald an acute abdominal catastrophe.

The case to be described here is of special interest not only because of the unusual onset of the disease with jejunal perforation and diffuse peritonitis, but also because the patient survived multiple jejunal perforation for almost a year. In addition to these features, the clinical picture was not complicated or over-shadowed in any way by the usual serious cerebral, cardiac, or nephritic symptoms so commonly occurring in polyarteritis nodosa. This absence of such severe complications enabled the progress of the intestinal condition to be observed and the response to treatment noted.

CASE REPORT

W. M., a man aged 41 years, had always enjoyed good health until two months before admission to hospital, when his general health began to fail and he noticed he became easily fatigued. On Jan. 6, 1954, he was suddenly seized with severe abdominal pain associated with vomiting and prostration. The pain persisted and became more widespread, and two days later he was admitted to hospital. He looked extremely ill, the tongue was coated and the breath fœtid. Pulse 128. Temperature 101·5°. There was generalized abdominal guarding, but tenderness and rigidity were most marked in the right iliac fossa. A diagnosis of general peritonitis was made, and the abdomen explored on the day of admission.

The lower abdomen was opened through a right paramedian incision, and the peritoneal cavity found to contain a considerable quantity of thin yellow pus. Scattered yellowish-white oval patches were present on the terminal ileum, and, though the lesions were somewhat suggestive of typhoid ulceration, on closer examination the appearances were certainly not typical of this condition. The appendix was normal. Owing to the patient's extremely poor condition further exploration of the abdomen was considered inadvisable. A specimen of pus was taken from the peritoneal cavity, and the abdomen closed with drainage. Continuous gastric suction and intravenous glucose-saline infusions were established, and 250,000 units of penicillin with streptomycin 0·5 g. were given six-hourly.

Since a diagnosis could not be made at operation, investigations were started post-operatively in an attempt to establish the cause of the peritonitis. The results were as follows :—

Pus from Peritoneum : Films : Moderate numbers of pus cells. No organisms or acid-fast bacilli seen. Culture : Sterile.

Blood-count : Hæmoglobin 97 per cent (Haldane)—14·3 g. per cent. White blood-cells 12,750 per cm. Differential count—Polymorphs 95 per cent, Lymphocytes 4 per cent, Monocytes 1 per cent.

Blood-culture : Sterile.

Blood Agglutinations :—

Widal : Agglutination of *S. typhi H* to titre of 1–160; Agglutination of *S. paratyphi B. H* to titre of 1–640; Agglutination of non-specific Salmonella to titre of 1–160.

T.A.B. response : No agglutination of *S. typhi O*; No agglutination of *S. paratyphi B. O*; No agglutination of *Brucella abortus*.

Clot Culture : Sterile.

Stool Examination : No pathogenic organisms. Occult blood-test negative.

Urine : Slightly turbid straw-coloured fluid. Reaction acid. Albumin nil. Sugar nil. Deposit, small numbers of leucocytes and epithelial cells. Very scanty hyaline casts. Urobilinogen—Ehrlich's test, large amounts; Schlesinger's test, positive. Bilirubin—Fouchet's test, negative.

In view of the equivocal results, it was assumed that the peritonitis was due to a perforation of small intestine consequent on some unusual form of intestinal ulceration.

The patient made a good recovery and was discharged from hospital after four weeks. He was kept under supervision as an out-patient and, except for occasional slight flatulence, was entirely symptom-free. Barium meal and follow-through examination showed no abnormality, and a cholecystogram was normal. Occult blood tests were negative on repeated stool examinations.

Three months later the patient was suddenly seized by an attack of abdominal pain with vomiting, and the clinical

features appeared to be identical to that of his first attack. After careful pre-operative resuscitation the patient was submitted to further laparotomy on April 16.

The abdomen was explored through a lower right paramedian incision excising the previous operation scar. The peritoneal cavity contained thick pus and some gas was present. Scattered over the entire gut there were small pale yellow plaques indicating ulceration of the underlying mucosa. The plaques were oval in shape, about 7 mm. in maximum diameter, and arranged with the long axis across the lumen of the bowel. These plaques tended to be at a point midway between the mesenteric and antimesenteric border of the gut. Each area was completely avascular, but was surrounded by a halo of vessels resembling in size and appearance those of a spider nævus. The jejunum was œdematous and showed a greater multiplicity of ulcers than were present in the ileum. The ileum was less swollen than the jejunum, and, though the ulcers were less numerous, they were larger in size. The cæcum showed a few lesions, but the pelvic colon did not appear to be involved. The stomach showed one or two small ulcers similar to those on the rest of the gut. The mesentery of the small gut was very swollen and was laden with fat of an outstanding canary yellow colour. Liver and spleen appeared normal. After examination of the entire intestine, a small perforation was discovered in the jejunum.

In view of the fact that the cause of these unusual recurrent ulcerations had not been established, it was decided to accept the grave risk of resecting the perforated ulcer together with an adequate length of jejunum, to enable a full examination and section of the gut to be carried out. About 6 in. of jejunum was resected and end-to-end anastomosis established. Following operation the patient was put on intravenous glucose-saline and gastric suction established. Penicillin 250,000 units and streptomycin 0·5 g. were given eight-hourly.

Pathological Report: The specimen consists of a resected piece of jejunum 7 cm. long with the attached mesentery. The fat of the mesentery appears an abnormal yellow colour and the peritoneal surface of the jejunum shows numerous yellow plaques each about 4–6 mm. in diameter. In one place there is a recent perforation 4 mm. in diameter. The vessels in the mesentery are hidden by fat, and, when dissected out, there were none of the nodular aneurysmal swellings which when present enable a diagnosis of polyarteritis to be made from the naked-eye appearance.

Microscopy: Sections taken from all parts of the specimen show a similar histological appearance. There is an extensive and severe polyarteritis which affects the small arteries and arterioles of the mesentery and throughout the wall of the intestine. The arteritis is focal in distribution but very extensive and very few arteries in the section show a completely normal appearance. The essential lesion is a panarteritis. The media in the affected vessels is necrotic, giving a strongly acidophilic staining reaction. There is an extensive infiltration by inflammatory cells extending throughout the vessel wall and out to a variable extent into the connective tissue surrounding the adventitia. The lesion is not confined to arteries and arterioles, as veins also are affected (*Fig.* 372). The inflammatory cells consist largely of polymorphs and leucocytes, but include eosinophils and macrophages. The effect of the arteritis upon the vessels is seen in various ways. Some arteries appear to be dilated as the result of stretching of the damaged wall; arteries are seen in which the lumen is blocked by proliferating fibroblasts (*Fig.* 373), presumably due to the organization of a thrombus formed during a previous attack, and in an occasional artery the media has split giving rise to a small dissecting aneurysm (*Fig.* 376).

Sections of the bowel wall taken through the yellow plaques observed beneath the surface of the peritoneum show a cellular exudate separating the peritoneum from the muscle. The inflammatory cells of the exudate are collected in denser aggregations around the subperitoneal arteries, all of which show arteritis; inflammatory cells accompany the branches of these arteries as they enter the muscle (*Fig.* 374). There is also a general infiltration of both muscle layers and submucosa by inflammatory cells, again with aggregations of cells in the vicinity of vessels showing arteritis (*Fig.* 375). The section taken through the edge of the perforation showed that it had occurred where a small artery affected by arteritis penetrated the muscle to join the submucosa. Presumably, the periarterial inflammatory reaction accompanying the vessel has given way (*Fig.* 376).

As soon as the section confirmed the diagnosis of polyarteritis nodosa, cortisone was given in doses of 25 mg. eight-hourly, later increasing to 50 mg. six-hourly. This administration resulted in very marked improvement of the patient's general condition and the temperature settled at once.

From this time onward the patient was kept on cortisone, and on occasion this was supplemented with ACTH. During this period careful watch was kept on the blood-chemistry, and the dose of cortisone regulated until a maintenance dose of 50 mg. six-hourly by mouth was found to be satisfactory. Potassium citrate was given by mouth in appropriate doses. On discharge from hospital on May 17 the blood-chemistry was as follows:—

Blood: Serum-sodium 320 mg.; Serum-potassium 18·5 mg.

Total serum-proteins 6·8 mg.; Albumin 4·0 mg., Globulin 2·8 mg.

Urine: Albumin, cloud. Deposit, moderate numbers of red blood-cells and a few granular casts.

Three days after discharge from hospital the patient was again admitted with another intestinal perforation, which on this occasion was treated conservatively by intravenous drip and continuous gastric suction together with streptomycin 0·5 g. six-hourly and ACTH 25 mg. six-hourly. Progress was quite satisfactory and the patient was discharged on June 7 on a maintenance dose of cortisone and ACTH, 25 mg. of each being given six-hourly by mouth.

The patient was kept under close supervision as an out-patient. Frequent blood examinations showed a serum-sodium varying between 300 mg. and 320 mg. (average 318) while the serum-potassium average was 15·8 mg.

Total proteins 6·0 mg.; Albumin 4·2 mg.; Globulin 1·8 mg.

Urinalysis showed occasionally a slight cloud of albumin, an occasional R.B.C., and a few casts, but on no occasion was there gross albuminuria. His general health was good and he was symptomless except for occasional colicky abdominal pain. He continued to take cortisone 100 mg. per day and was able to do normal work.

On Aug. 11 he complained of the sudden onset of upper left-sided abdominal pain and vomiting; there was upper abdominal rigidity and it was assumed that he had suffered another small intraperitoneal leak. This settled down in a few days with conservative measures.

On Sept. 27 the patient reported for routine examination. He stated that he was in perfect health and was back to full working duties. It was observed that he had two small areas on the face where there was thickening of the epidermis: the appearance rather resembled that of a small basal-cell tumour before the onset of ulceration. One of these areas was excised on the assumption that the lesion was further evidence of polyarteritis nodosa. The section was reported on as follows:—

Pathological Report: There is no evidence of polyarteritis in the few vessels included in the biopsy. The picture is that of atrophy. The epithelium is

thin and the papillæ are poorly developed. The site of the ulcer is not denuded of epithelium but the epithelium is thinned down to a flattened malpighian layer with a superficial thin covering of keratin. The collagen fibres in the dermis are relatively acellular and show hyaline degeneration.

FIG. 372.—Small artery in the mesentery affected by panarteritis. The accompanying vein is similarly affected. (× 50.)

FIG. 374.—Section through peritoneal and muscular coats of the jejunum. The peritoneum is separated from the muscle by a cellular inflammatory exudate. Collections of inflammatory cells are seen around two subperitoneal vessels which show arteritis and these cells extend along the branches of these vessels as they enter the muscle. There is also a general infiltration of the muscle by inflammatory cells. (× 72.)

Six days later the patient was again admitted with another perforation. The operative findings were exactly similar to those found previously. The site of perforation was again in the jejunum. Similar suture was carried out and the abdomen drained. It was noticed at this stage that further skin lesions had appeared over the chest, neck, face, and extensor aspects of the forearms. The lesions now showed deeper central depression and closely resembled multiple rodent ulcers.

Recovery from the perforation was quite uninterrupted, but twelve days later, on Oct. 14, the patient sustained another larger jejunal perforation necessitating further operation. At this operation the previous wound was excised for section to provide the opportunity of studying wound healing, as at this time the patient was on 50 mg. cortisone six-hourly. The report on this section was: "There seems to be a normal reaction to wound healing with no evidence of periarteritis."

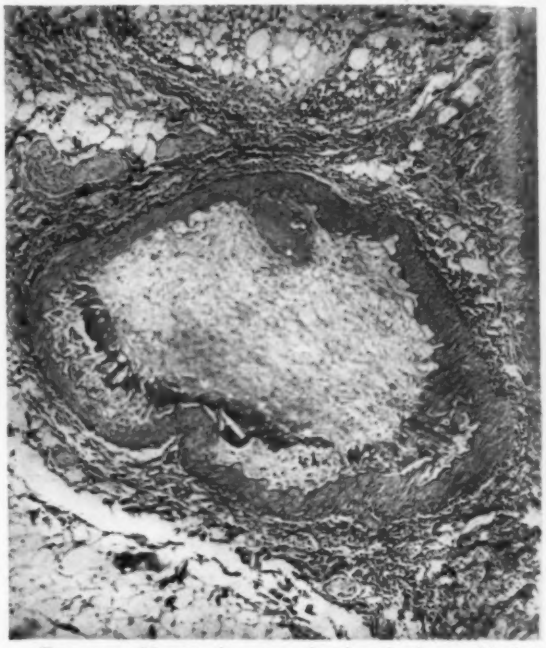

FIG. 373.—Mesenteric artery showing the lumen blocked by proliferating fibroblasts. Presumably these represent the organization of a thrombus formed during a previous attack. (× 60.)

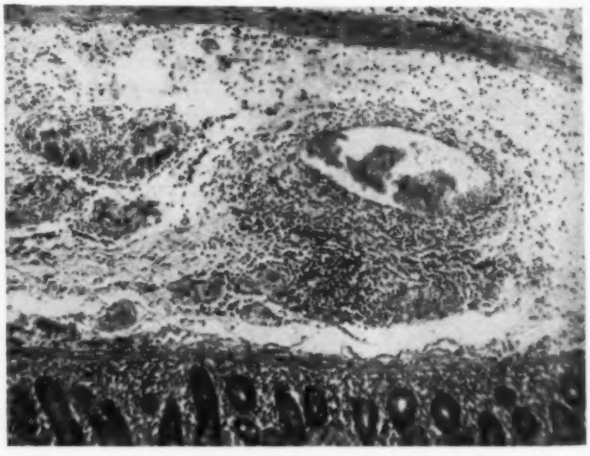

FIG. 375.—Collections of inflammatory cells around vessels in the submucosa. (× 10.)

Following this last operation progress was not entirely satisfactory, the patient became more toxic and jaundice appeared. At this time the blood-chemistry was as follows :—

Serum-potassium and serum-sodium showed a falling off—serum-sodium from 310 to 290 mg., and the potassium varied between 12·5 and 15·7. Blood-urea 13 mg.

On Nov. 5 the patient had a coronary thrombosis and died in a few hours.

DISCUSSION

It has long been recognized that symptoms referable to the gastro-intestinal tract are present in a large proportion of cases suffering from polyarteritis nodosa. In a review of 30 cases admitted to the Mayo Clinic between 1926 and 1946, Wold and Baggenstoss (1949) found that 76·6 per cent had abdominal symptoms. The significance of the abdominal complaints was, however, difficult to interpret, since in a proportion of cases suffering from abdominal pain no explanation for these could be obtained at post-mortem examination. In another group patients suffering from polyarteritis affecting the viscera did not complain of abdominal pain, though the typical lesions of polyarteritis nodosa were found in the intestinal tract when death had resulted from other causes. All the lesions that were studied could be attributed to interference with the blood-supply to the affected organ. Infarction was by far the commonest lesion, and when this occurred ulceration and hæmorrhage frequently resulted.

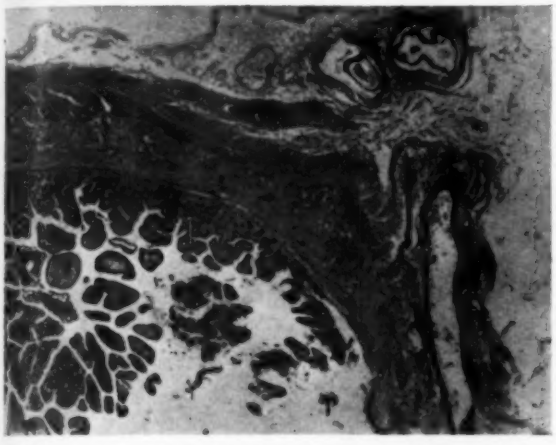

FIG. 376.—Section through the wall of the jejunum at the edge of the perforation. At the site of perforation an affected artery penetrates the muscle to reach the submucosa; presumably the collapse of the inflammatory tissue surrounding this artery was the cause of the perforation. Note the subperitoneal artery showing a dissecting aneurysm in the wall. (× 10.)

The occurrence of abdominal symptoms in polyarteritis nodosa has also been emphasized by Spiegel (1936), who reviewed in detail 17 cases of the disease. Five of these cases presented the clinical features of acute appendicitis and the correct diagnosis was not made until after operation. Fifteen of the series showed gastro-intestinal ulceration at post-mortem examination. The ulcers were multiple and situated at any point throughout the entire length of the intestinal tract. In only 3 cases was this ulceration a feature of clinical importance. Of these 3 cases, 1 case had severe colonic hæmorrhage, 1 case was thought to be suffering from ulcerative colitis, while in 1 case fæcal peritonitis had resulted from perforation of a jejunal ulcer in a patient already gravely ill with hypertension, advanced arterial disease, and kidney failure.

In the case here described, though there was some slight failure of general health, there were none of the prodromal symptoms so commonly found in polyarteritis. There was no history of muscle pains, upper respiratory infection, or allergic manifestations. The case virtually presented as an acute abdominal emergency, with fæcal peritonitis due to perforation of a jejunal ulcer.

The outstanding feature of this case is that over a period of eleven months the patient sustained and survived no less than six perforations of the jejunum.

Table I.—SUMMARY OF EPISODES OF INTESTINAL PERFORATIONS

DATE	ABDOMINAL EMERGENCY	TREATMENT	ACTH AND CORTISONE
1954—			
Jan. 6	Jejunal perforation	Suture	—
April 16	Jejunal perforation	Resection of ulcerated gut	Cortisone 75 mg., increasing to 200 mg.
May 20	Jejunal perforation	Conservative treatment (with drip and suction)	ACTH 100 mg., cortisone 100 mg.
Aug. 11	Jejunal perforation	Conservative treatment	ACTH 100 mg., cortisone 100 mg.
Oct. 12	Jejunal perforation	Suture	Cortisone 200 mg.
Oct. 14	Jejunal perforation	Suture	Cortisone 200 mg.
Nov. 5	Died	—	—

On four occasions the perforation had resulted in severe diffuse peritonitis necessitating operative treatment, while on two occasions the leak was of less severity and a satisfactory outcome resulted from conservative management by intravenous drip therapy and gastric suction. The episodes of perforation are outlined in *Table I.*

Versé (1907) reported a case of periarteritis with rupture of ileal and jejunal ulcers, and Gruber (1917) reported a further case of rupture of the jejunum. We have been unable to find in the literature any report of a case which has survived multiple perforations with fæcal peritonitis.

The survival of this patient for almost a year has provided a unique opportunity to observe the clinical progress of intestinal ulceration, in the first instance before the administration of cortisone and ACTH, and subsequently when cortisone therapy was given after the second perforation.

Following the first perforation in January, 1954, the patient made a steady recovery and remained symptom-free for three months. At this stage the diagnosis was not established and consequently no cortisone was given. After the second perforation when a portion of gut was resected and the diagnosis made, the patient's convalescence was greatly accelerated by the use of cortisone in doses of 75–200 mg. per day. In spite of this dramatic improvement subsequent to the administration of cortisone, the patient developed a further jejunal perforation three days after discharge from hospital and while still on maintenance doses of cortisone. Subsequently, three further jejunal perforations occurred in spite of adequate cortisone and ACTH therapy.

It is interesting to note that increasing the dose of cortisone, and supplementing this with ACTH, failed to prevent further jejunal perforation. In considering the causes of this failure of therapy, it is assumed that if the dose of cortisone is inadequate the disease progresses and intestinal ulceration

persists, with the hazard of further perforation. On the other hand, if following an adequate dosage the arterial lesions heal, thrombosis may occur in the healing vessels and result in perforation of the ulcer because of ischæmia. In this respect therefore cortisone therapy may prove to be a double-edged weapon, as pointed out by Drury, Hickey, and Malone (1951).

It is also interesting to note that seven months after the onset of symptoms the patient developed skin lesions. These closely resembled rodent ulcers in appearance, and showed varying degrees of activity from time to time. Section of the lesions did not show the typical arterial changes of polyarteritis nodosa, but there was no doubt that when these lesions become most florid the intestinal lesions were also more active and perforation occurred. It may well be that the skin lesions were due to colloid degeneration in the tissues and not consequent on interference of the arterial supply (Spiegel, 1936).

Another feature of interest is that the anticipated deleterious effect of cortisone on wound healing was not borne out in actual fact. The penultimate perforation which occurred on Oct. 2 was followed twelve days later by further perforation. This final perforation provided the opportunity to excise a twelve-day-old wound and to examine it microscopically for signs of wound healing. Healing was found to be entirely normal on wound section.

COMMENT

From a review of the literature and from the considerations discussed above, it would appear that abdominal pain is frequently present in cases of polyarteritis nodosa. In most cases the symptom is of minor importance and is overshadowed by the other manifestations of the disease. It is, however, apparent that symptoms can be of such severity as to simulate surgical conditions within the abdomen.

Gastro-intestinal ulceration is commonly found at post-mortem examination, but is usually of minor importance. In the case described jejunal ulceration with perforation was the major feature. The tendency to repeated perforations was most marked and the limitations in the value of cortisone and ACTH were clearly illustrated.

I gratefully acknowledge the help and assistance of Dr. P. N. Coleman, who supplied the photomicrographs and the pathological report.

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VERTICAL COMPRESSION INJURIES OF THE CERVICAL SPINE

BY P. N. ROBSON, NEWCASTLE UPON TYNE

ALTHOUGH in recent years several papers have been devoted to cervical spine injuries, little work has been published on those due to vertical compression.

V. H. Ellis (1946) described a case of vertical fissure fracture of a vertebral body due to one of these injuries.

The largest series of vertical compression injuries of the cervical spine was reported by Richman and Friedman (1954), who discussed the radiographs of 17 cases seen in a paraplegic unit some months after the original injury. They considered that a vertical fissure-fracture of the vertebral body in the anteroposterior radiograph was pathognomonic of a vertical compression injury, and published a number of radiographs demonstrating this lesion. The value of tomography in showing these fissures was stressed, also the occurrence of this injury in two adjacent vertebræ was noted. In the above paper a backward displacement of the upper vertebral body on the lower was described (⅜ in. in their *Case* 4), but no lateral radiographs were reproduced.

This paper reports 4 cases of vertical compression injury of the cervical spine with post-mortem findings; one of these cases was successfully treated by early bone-grafting after reduction by traction.

CASE REPORTS

Case 1.—A window cleaner was admitted to the unit after having fallen from a ladder on which he had been cleaning a first-floor window, and landed on his head in a bed of soil. He was found to have a complete paresis and sensory loss below the sixth cervical level. Radiographs showed a fracture-dislocation of the fifth cervical vertebra. The anteroposterior radiograph showed a small vertical fissure in the fifth vertebral body. In the lateral view there was gross crushing of the anterior portion with displacement of the intact posterior part backwards across the spinal canal (*Fig.* 377). There was no overlapping of the facets.

The cervical spine was immobilized in plaster and the patient was transferred to the paraplegic unit, where he is still surviving after four years. There has been no recovery of voluntary power or sensation.

Case 2.—A regular Army corporal, aged 32, was admitted 12 hours after he had been involved in an accident while on duty. It was stated that he tripped over a low bed and fell onto his head. He had a 2-in. laceration over the vertex of his skull with much local bruising, so a vertical compression injury was assumed to have occurred. There was a complete quadriplegia below the sixth cervical level. Radiographs of the cervical spine (*Fig.* 378) were similar to those in *Case* 1, showing crushing of the anterior part of the fifth vertebral body with backward displacement of the intact posterior fragment. The anteroposterior view showed a

well-marked vertical fissure-fracture of the fifth vertebral body. Death occurred some 24 hours later.

POST-MORTEM FINDINGS.—The cervical spine was removed intact. There was a large retropharyngeal hæmatoma which accounted for the greatly increased soft-tissue shadow seen in the lateral radiograph. The spinal cord was completely crushed at the level of the injury. The spine was sectioned and showed gross

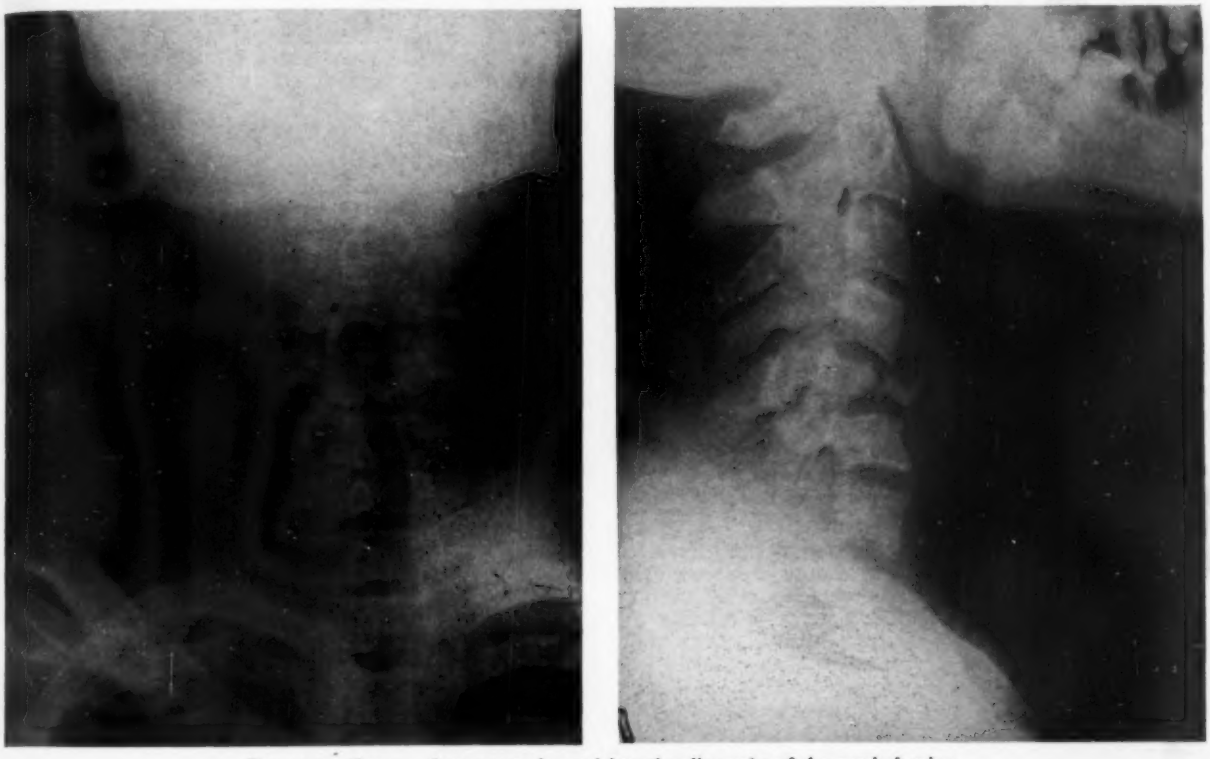

FIG. 377.—*Case* 1. Anteroposterior and lateral radiographs of the cervical spine.

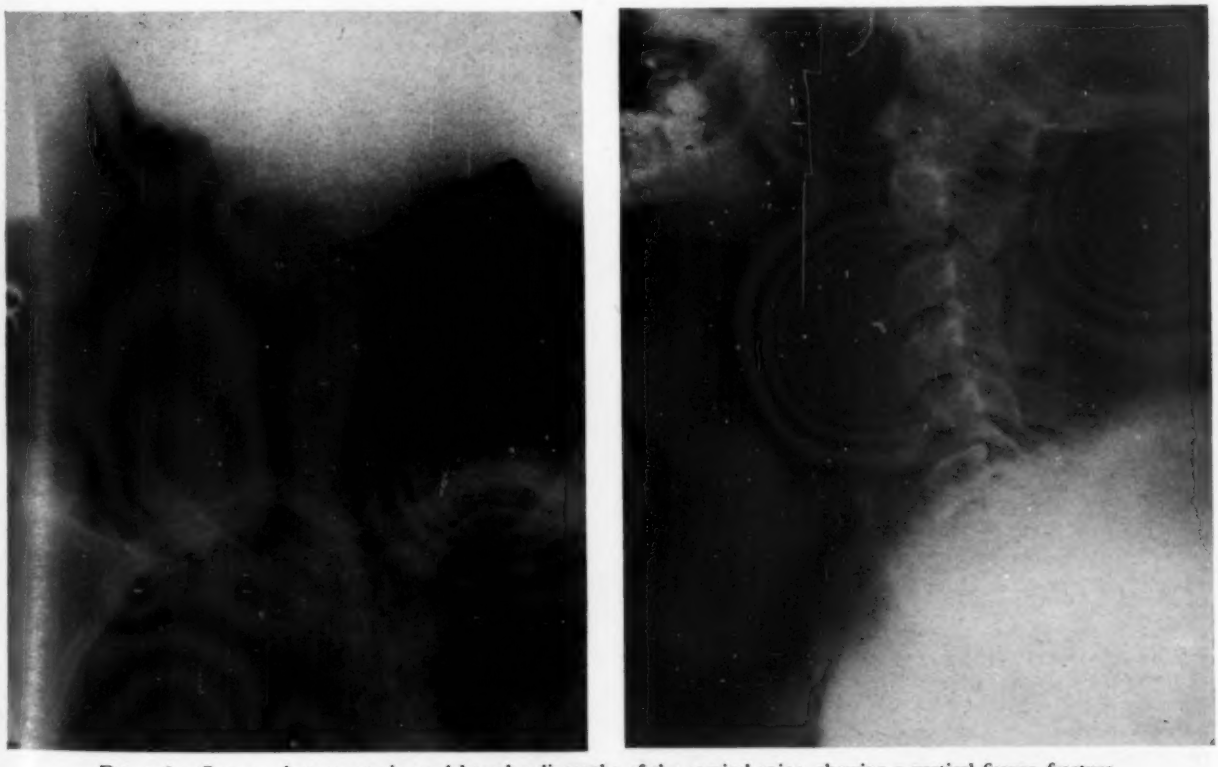

FIG. 378.—*Case* 2. Anteroposterior and lateral radiographs of the cervical spine, showing a vertical fissure fracture of the body of C.5.

crushing of the anterior portion of the vertebral body with an intact posterior triangular portion. *Fig.* 379 shows the same specimen with a small vertical compression force applied by a rubber band, demonstrating the displacement of the intact posterior portion of the body backwards across the vertebral canal.

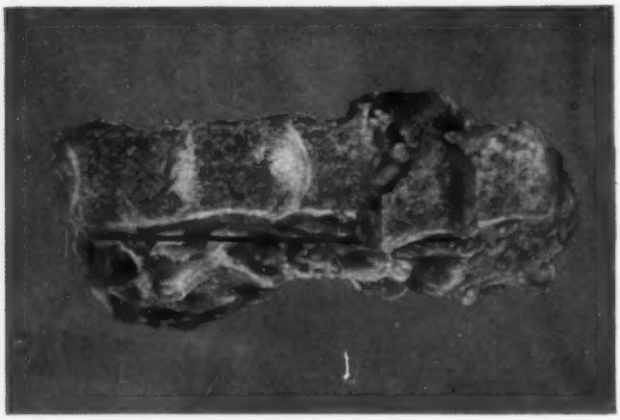

FIG. 379.—*Case* 2. Sagittal section of the cervical spine with vertical compression by a rubber-band to show the typical displacement.

Case 3.—A young man, a Powderhall sprinter, aged 21 years, was admitted following a motor-cycle accident. While riding he had hit the kerb, whereupon the machine stopped suddenly but the patient went on in a horizontal position until stopped by his head hitting a lamp-post. On admission he had a complete quadriplegia below the sixth cervical level. Radiographs of the cervical spine (*Fig.* 380) showed a fracture-dislocation of the fifth cervical vertebra with backward displacement. No vertical fissure-fracture was seen in the anteroposterior view, but tomographs were not taken. Death occurred some 24 hours later.

POST-MORTEM FINDINGS.—There was a fracture-dislocation of the fifth on the sixth cervical vertebra, with gross crushing of the anterior portion of the fifth vertebral body, the intact posterior part being displaced backwards across the spinal canal with pulping of the spinal cord. On sagittal section the appearances of the vertebræ were exactly similar to those of *Case* 2.

Case 4.—A man, aged 29 years, was admitted after a mining accident in which he was struck on the vertex of his skull by a coal-cutting machine. He was complaining of severe pain in the neck.

ON EXAMINATION.—There was a 1-in. laceration of the vertex of the skull where he had been struck. There was gross limitation of neck movement with severe pain. There was no evidence of neurological damage, all muscle groups were active, and there was no sensory loss. Radiographs (*Fig.* 381) showed a vertical compression fracture of the fifth and sixth cervical vertebræ with backward subluxation of the fifth on the sixth. In the anteroposterior view there was a small vertical fissure-fracture in the sixth vertebral body.

In view of the unstable nature of this fracture-dislocation skull traction was applied with 10 lb. of traction. This traction was maintained for three weeks. At the end of this time a Minerva plaster-of-Paris jacket was applied with the neck in hyperextension. Radiographs showed that the reduction had been maintained. One week later a window was cut in the plaster and spinal fusion was carried out, the fifth, sixth, and seventh laminæ being fused by cancellous grafts from the posterior iliac crest (Mr. C. G. Irwin). The wounds healed by first intention. Immobilization was maintained for four months, when radiographs showed sound fusion.

Three months later there was an almost full range of painless neck movements and the patient had returned to his work in the coal mines. At follow-up one year later

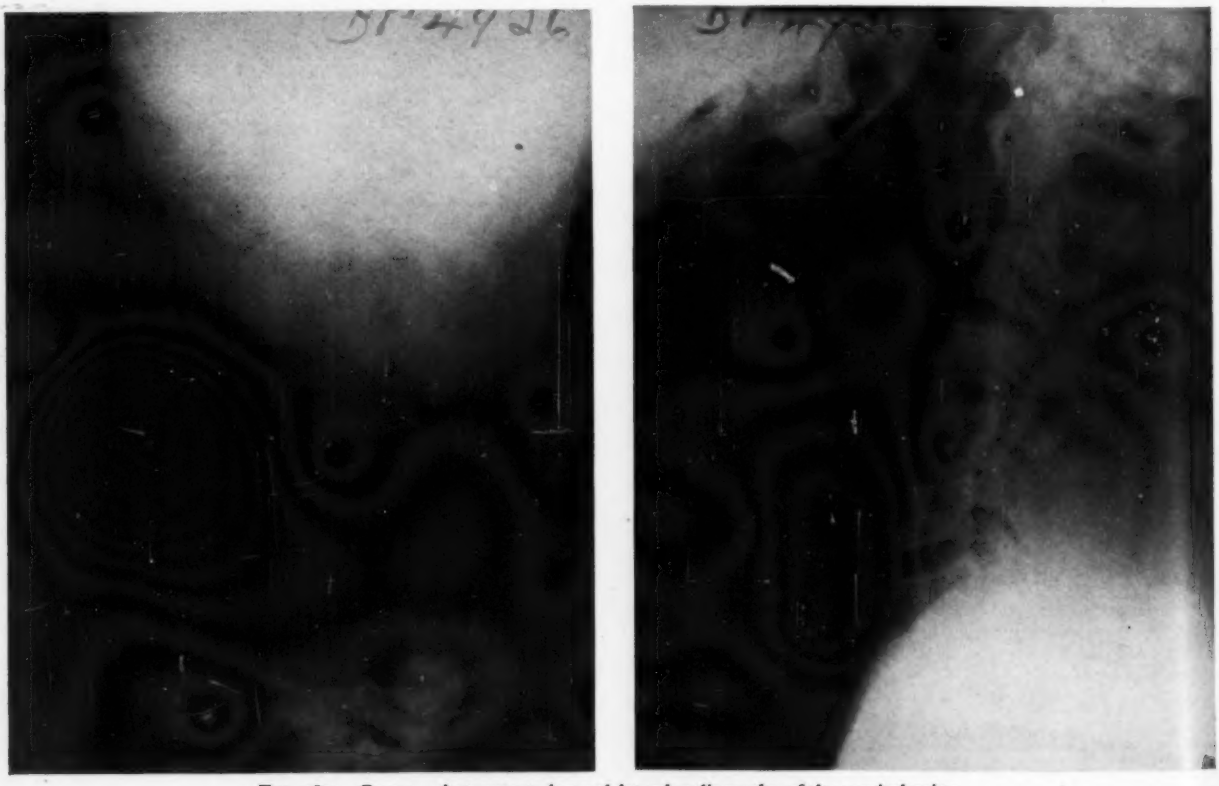

FIG. 380.—*Case* 3. Anteroposterior and lateral radiographs of the cervical spine.

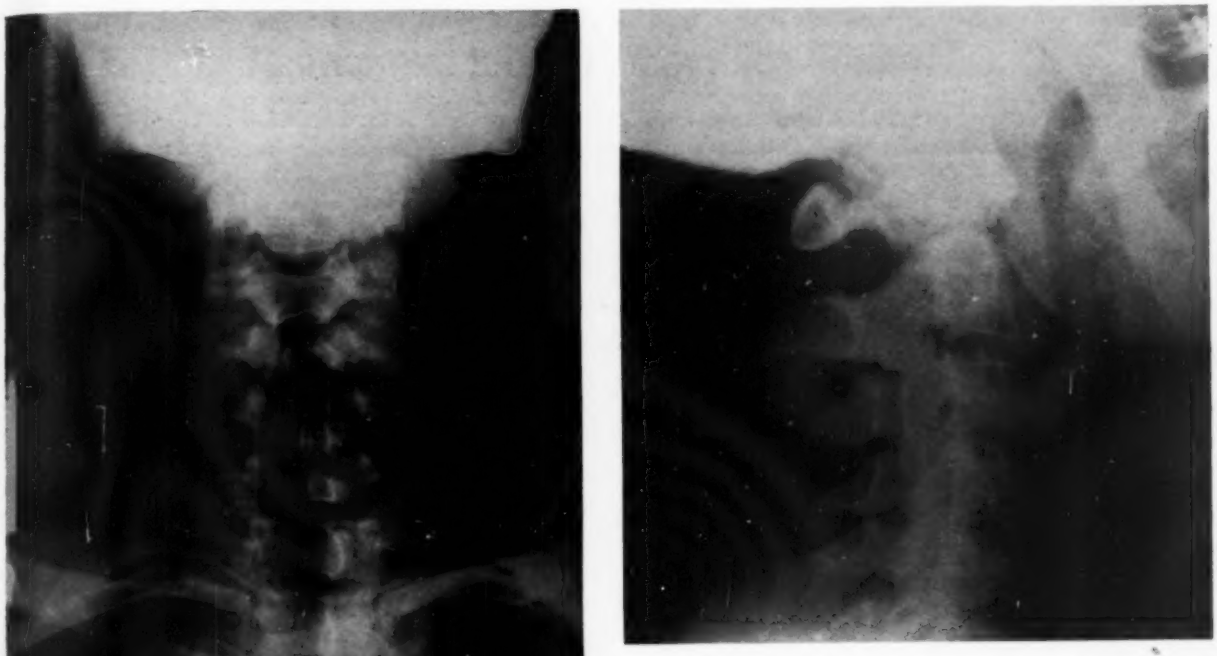

FIG. 381.—*Case* 4. Anteroposterior and lateral radiographs of the cervical spine.

there were no complaints referable to his neck and he was still at work. Radiography showed solid fusion of the grafts, but slight posterior subluxation of the fifth on the sixth cervical vertebra persists (*Fig.* 382).

COMMENT

This vertical compression fracture-dislocation of the cervical spine differs in both mechanism and displacement from the commoner flexion injury. There is severe crushing of the anterior part of the vertebral body, but the posterior portion remains intact and is displaced backwards across the spinal canal, crushing the cord in severe cases. All cases reported here were confined to the lower cervical vertebræ, chiefly the fifth. Reduction of the displacement was accomplished by traction to overcome the pull of the cervical muscles which maintains the displacement as shown in *Fig.* 379. It was noted that in both post-mortem specimens the reduction was stable in hyperextension owing to the shape of the intact posterior fragment of the vertebral body. Reduction was maintained in this position in *Case* 4.

V. H. Ellis (1946) suggested that in view of the well-known tendency to recurrence of the flexion fracture-dislocations, early operative fixation two weeks after the injury, by wiring and bone-grafting, was desirable. In our case wiring could not help to maintain reduction, but early stabilization by bone-grafting was essential to provide stability, the reduction being maintained by hyperextension in plaster while the grafts fused.

I am grateful to Mr. C. Gordon Irwin for permission to publish these cases, and to Dr. Whately Davidson for permission to publish the radiographs.

FIG. 382.—*Case* 4. Lateral view of cervical spine, showing solid fusion of the graft.

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RHINOSPORIDIOSIS OF THE BRONCHUS

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RHINOSPORIDIOSIS is a fungous infection affecting mainly the skin and the mucous membranes. We are presenting a short review of the literature and recording as far as we can determine the case record of the first reported occurrence in a bronchus. The patient was subjected to bronchoscopic removal followed by a bilobectomy. In addition he had shown multiple sites of infection elsewhere in the body.

The increasing literature on rhinosporidiosis bears out the fact that it is a widespread disease. Though the majority of cases are reported from India, it has been recognized in many other parts of the world, such as South America, the United States, England, Egypt, South Africa, Ceylon, and the Philippines. As far as we are aware, 460 cases have so far been reported from India alone; it appears to be especially common in South India. D. Bhaskara Reddy (1954) reviewed the material obtained from 156 biopsies that were examined in the Madras Medical College, the largest series so far recorded. Purandhare and Deoras (1953) from Bombay analysed material from 100 cases. Allen and Dave (1936) studied the treatment based on 60 cases that were seen over a period of eighteen months in the Central Provinces of India (Madhya Pradesh). So far 54 cases have been recorded at the Christian Medical College Hospital, Vellore.

J. Wright, in 1907, reported from America the first case on which an operation to remove the lesion had been done ten years previously. In 1925, V. Denti published the first case reported from Europe, which occurred in an Italian woman. Mackenzie, in 1933, gave the first description of its occurrence in an Englishman, who gave a history of having been in India for a long period. As far as we know the case here presented is the first one reported with infection in the bronchus as well as in other foci.

There is a certain air of romance attached to the name 'Rhinosporidium'. The condition was first observed by Professor Malbren, of Buenos Aires, in 1892. In 1896 Seeber re-examined this material and included it in his thesis for the M.D. degree, but failed to name it. Belou, in 1903, designated the organism as *Coccidium seeberi*, though Wernicke apparently had suggested the name in 1900. The first case recognized in India was by O'Kinealyi in 1894. Minchin and Fantham in 1905 reviewed the material of O'Kinealyi's case and called the organism *Rhinosporidium kinealyi*, being unaware of the fact that it had earlier been named *Coccidium seeberi*. Ashworth (1923), after a study of Rhinosporidium, proved that it was not a sporozoa, but belonged to the group Phycomycetes in the sub-order of Chytridineae, and called it *Rhinosporidium seeberi*, which has become its accepted name.

The organism is a round or oval spore measuring 6–7 μ in diameter. It has a well-defined limiting membrane in which are enclosed vacuolated cytoplasm, and a nucleus and nucleolus. Mitotic nuclear division takes place with concomitant increase in size of the organism. As many as 16,000 young spores can be found inside a sporangium by the time it has reached a size of about 200 μ. At this stage it bursts through a pore, with liberation of the young spores together with some mucoid material. Attempts to culture the parasite have hitherto been mainly unsuccessful. Dhayagude (1941) kept the parasite in a well-preserved state for about three months on a combination of Lowenstein's and potato-water media. Iyer, working in Guindy, Madras, reported a yeast-like growth isolated from a case of rhinosporidiosis, but details of the technique employed are not available. Rao (1938) obtained a positive culture using horse-dung agar, and later subcultured on Sabouraud's medium containing dung juice. Rao and Iyer separately have reported rhinosporidiosis in cattle and horses. Most of the bullocks in which the condition was detected were those used in agriculture. Animal inoculation has not so far been achieved.

The exact mode of infection is still unknown. The possibility of direct transmission was suggested by Ashworth (1923) and that of waterborne infection by Wright in 1922. Mandelik (1937) observed that a majority of his patients were sand divers employed in localized areas of the river and tanks near Poona, India. He suggested that there was a close relationship between this occupation and infection, but Noronha (1933) could not isolate the organism from the water. Further support to the theory of waterborne infection was given by Allen and Dave (1936), who thought that there was a relationship between Rhinosporidium and Ichthyosporidium which infects salmon. They were under the impression that Rhinosporidium, being allied to Ichthyosporidium, lived as a parasite or saprophyte of fish and that man got infected through water where such fish lived. A significant number of patients do not give a history suggestive of waterborne infection and further work is necessary to find out the exact mode of infection. This problem is complicated by the inability so far to cultivate the organism satisfactorily.

The disease appears to be much more common in males than in females. There were 404 males and 56 females out of 460 cases reported so far in India. In Bhaskara Reddy's (1954) material the ratio of males to females was 9 : 1; in that analysed in the Christian Medical College Hospital, Vellore, it was 2 : 1. It occurs most frequently in the age-group 15 to 35 years. The youngest reported case was in a 17-year-old patient, the oldest being an 82-year-old male Ceylonese. The exact relationship of trauma to the infection with Rhinosporidium cannot be ascertained. The frequency of recurrences after treatment is an argument in support of the traumatic theory. Probably this is due, in many cases, to incomplete removal of the infection. More than one member of a family may be infected;

whether this is due to a common source of infection or to one member of the family infecting others is not clear. There are reports of cases where members of a family living in close contact with the patient have not been infected.

The nose is the most common site of infection. The nasopharynx, lacrimal sac, larynx, and conjunctiva are affected in this order of frequency. Infection of the urethra, penis, soft palate, and parotid gland have been reported. Multiple sites of infection may be present. Dhayagude (1941) reported a case where there was generalized rhinosporidial granulomata all over the body. The infection may appear as a pedunculated or sessile tumour or as a combination of these two. Probably a breach in the mucosa is essential for the Rhinosporidium to become established.

In the nose it usually appears as a reddish papillomatous growth resembling a ripe strawberry. As it grows, it may protrude through the nostril, showing a lobulated appearance. If it arises from the posterior part of the nares, it may hang into the pharynx. Sometimes it may be of more solid consistency, showing a resemblance to a ripe fig. On close scrutiny white spots are found on the surface of the mass which are the actual sporangia. The growth bleeds readily on interference. In the larynx the appearance may be villous, papillomatous, or myxomatous. Obviously these growths, being so common in the upper respiratory passages, may infect the tracheobronchial tree lower down, as in the case reported here.

The nasal growth leads to irritation and the sensation of a foreign body in the nose. There is usually a thin, mucoid discharge with frequent bleeding; blocking of the nose with difficulty in breathing is common. More serious difficulty is encountered when the mass protrudes into the pharynx or arises in the larynx. Watering of the eyes is frequent if there is involvement of the lacrimal sac. Rhinosporidium has to be thought of in the differential diagnosis of any asymptomatic growth in the eye. When there is infection of the tracheobronchial tree, the patient may complain of cough with mucoid sputum. There may be a history of frequent bouts of hæmoptysis, though this may be small in quantity. The growth in the bronchus may act as a valve during respiration, especially if it has a pedicle. A wheeze may be heard or the patient may suddenly complain of dyspnœa due to atelectasis or emphysema. Secondary infection distal to the site of obstruction may lead to bronchiectatic changes or to the formation of a lung abscess. The patient may even expectorate small masses of the Rhinosporidium.

Histological study shows the covering of the tumour mass to be stratified squamous or ciliated columnar epithelium or a mixture of both (*Fig.* 383). There are usually vascular papillary processes with a core of fibrous tissue; myxomatous tissue may also be found. The spores of Rhinosporidium are usually seen in between the papillary processes, lying loose in the stroma and more towards the surface. In some places the sporangia appear to have burst through the covering epithelium. Polymorphonuclear leucocytes and lymphocytes are seen distributed throughout these lesions, though polymorphonuclear leucocytes have a tendency to crowd around the spores. Giant cells, usually of the foreign-body type, are found around a degenerating sporangium, while they may occasionally be seen inside a big sporangium; they may be observed to have engulfed a few spores. There may be evidence of hæmorrhage either fresh or old. No spore has so far been seen invading or inside a blood-vessel. Karunarathne (1939) reported a case where carcinoma had supervened, while in another case he noticed associated molluscum contagiosum alongside rhinosporiosis of the eyelid.

FIG. 383.—Showing the papillary processes in which the spores of the Rhinosporidium are seen. (× 50.)

By rubbing the growth on a glass slide and examining it under the low power of a microscope, the typical spores will be seen. Examination of the sputum may also show the spores, as in the case reported here. Romanowsky's and iron-hæmatoxylin stains are suitable.

Since the growth appears to show no evidence of infiltration of the deeper layers, excision of the infected areas seems to be the treatment of choice, but that it is not always curative is shown by the frequency of recurrences. Recurrence appears to be more common if the lesion is extensive or is found in multiple sites. Being frequently situated in the upper respiratory tract, pieces may become dislodged during the process of removal and gain entrance to the tracheobronchial tree, leading to implantation in this new site. The antimony group of drugs are said to be useful, though their curative value has not been accepted. Antibiotics apparently have no action on the parasite.

CASE REPORT

A. N., C.M.C.H. 123962, male, aged 31 years, attended the out-patient department of the Christian Medical College Hospital, Vellore, South India, on Aug. 1, 1952, with a history of a growth in the nose which bled frequently during the past fifteen years. In 1950 and 1951 attempts at the removal of the growth from the nose were made. He also had a course of ureastibamine injections. For the past one year he had cough with

dyspnœa and occasional fever. There was slight mucoid expectoration, but he had had no hæmoptysis. He had been given 41 g. of streptomycin on the assumption that he had pulmonary tuberculosis. He was referred to the Ear, Nose, and Throat Department, where on examination

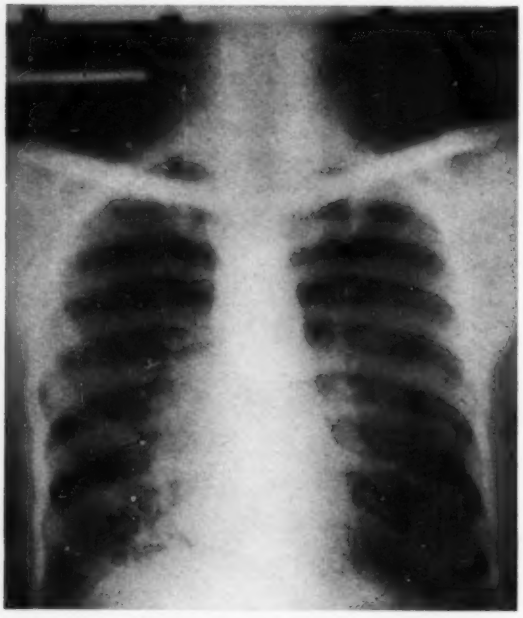

FIG. 384.—Radiograph of the chest showing increased haziness over the right lower lobe.

rhinosporidiosis was found in both nostrils arising from the septum and left middle and inferior turbinates. There was also a similar growth in the nasopharynx obscuring both choanæ. He had a soft swelling in the

FIG. 386.—Spores seen extending into the submucosa on microscopical examination. (× 25.) Bronchial wall is also well seen.

left canthus. There were diminished breath-sounds at the bases of both the lungs, with a few râles.

He gave a family history of his mother having had similar complaints. His two brothers, who do not live with him, also have the same complaint.

He received a short course of penicillin injections, 500,000 units in oil, daily from Aug. 7 to Aug. 18. On Aug. 25 he was admitted on the Thoracic Service for investigation of the cough. A radiograph of the chest showed slight haziness over the right lower lobe (*Fig.* 384). A bronchoscopy was done on Sept. 1, when a pedunculated mass was seen just below the level of right upper lobe orifice in the right main bronchus. Biopsy of it showed Rhinosporidium. There was not much bleeding on

FIG. 385.—The resected specimen of the right middle and lower lobes with the granulomatous lesion in the wall of the superior and basal segmental bronchi of the lower lobe.

taking a biopsy from the growth. On Sept. 9 a bronchography was done, but there was not a satisfactory filling of the right middle and lower lobe bronchi owing to the mass obstructing the right bronchial lumen just below the right upper lobe bronchus. Radiographs of the sinuses showed haziness of both the maxillary sinuses. Re-bronchoscopy done on Sept. 27 showed an adequate lumen of the right bronchus. It was decided to attend to the lesions of the upper respiratory tract before the mass in the right bronchus could be dealt with, as otherwise there was every chance of further spread down the lower respiratory passage from nose and nasopharynx.

On Oct. 7 he underwent submucosal resection with removal of the rhinosporidial mass situated in the nostrils. On Oct. 27 the growth in the nasopharynx was removed by a transpalatal approach and the base was coagulated. This was followed up on Nov. 8 with left dacrocystectomy and the lacrimal sac that was removed showed rhinosporidiosis.

Examination of the sputum on Dec. 4 revealed Rhinosporidium. Bronchoscopy done the same day showed an increase in size of the mass obstructing the right intermediate bronchus. An attempt was made to remove as much of the mass as possible. Microscopical examination of the mass removed showed pseudostratified ciliated epithelium covering connective tissue containing typical sporangia. Many areas showed a collection of foreign body giant cells and chronic inflammatory cells. On Dec. 16 he underwent a right thoracotomy. It was decided to determine whether or not a local removal of the mass was possible. Therefore a bronchotomy of the right intermediate bronchus was done and it was found that the mass of Rhinosporidium extended over the origin of the segmental bronchi of the right lower lobe. The right upper lobe bronchus appeared normal. The upper lobe parenchyma felt normal. Local removal of the mass was done but this appeared to be unsatisfactory. A right middle and lower

lobectomy was carried out with division of the right intermediate bronchus above the uppermost limit of the tumour.

Examination of the resected lobes showed in the intermediate bronchus, and extending into the superior segment of the lower lobe and for a short distance into the basal segment of the lower lobe, a granulomatous lesion adherent to mucosa (*Fig.* 385). There was no evidence of bronchiectasis in the resected lung. Microscopical examination of the area of the bronchus where the granular area was found showed pseudostratified columnar epithelium which had ulcerated in places. Scattered under this, and extending deeper down into the submucosa almost up to the cartilage, were numerous sporangia of varying size, some with single spores, others with numerous spores (*Fig.* 386). The chitinous coat was thickened in some of the sporangia. A few were seen rupturing on the surface of the mucosa. The submucous fibrous tissue was increased in amount. Diagnosis : Rhinosporidiosis of the bronchus.

Post-operatively he developed transient atelectasis of the right upper lobe. Bronchoscopic aspiration was done and the lung well aerated again. He was discharged on Jan. 20, 1953.

He was readmitted on the Ear, Nose, and Throat Service twice—on Sept. 18, 1953, and July 1, 1954—when he had further removal of the Rhinosporidium which had recurred in the nose and the nasopharynx. Following the attempt at removal of Rhinosporidium by avulsion and cauterization of the base, 15 mg. radium was applied to the nasopharyngeal region.

On March 25, 1955, he was readmitted for a check up of the lungs and the bronchial tree. A radiograph of the chest showed clear lung fields. Bronchoscopy revealed no evidence of Rhinosporidium in the bronchial tree. There was further recurrence of the mass in the nose, however.

CONCLUSION

The literature on rhinosporidiosis has been reviewed, and so far as is known the first case of rhinosporidiosis of the bronchus has been reported. It is obvious that the bronchial involvement in this case has been due to the implantation of the parasite from the upper respiratory tract. However, it should be possible for the bronchus or the pulmonary parenchyma to be the primary site of infection. In endemic areas such a possibility should be borne in mind when confronted by a patient whose presenting complaints and symptoms are entirely pulmonary. In every case of suspected pulmonary rhinosporidiosis a radiograph of the chest and bronchoscopy becomes a necessary procedure. Examination of the sputum and bronchial washings for the parasite has a place in suspected cases of rhinosporidiosis of the tracheobronchial tree.

In our case it was decided to attempt surgical removal of the lesions in the nose, nasopharynx, and the lacrimal sac before effecting a radical removal of the pulmonary lesion.

Whether resection of the lobes was necessary in this case or a bronchotomy and excision of mass with cauterization of the base would have been enough has been a question we have asked ourselves. At the time of operation there was no way of knowing if the lung beyond the bronchial site contained exfoliated parasites which could be responsible for recurrence. Pathological examination of the bronchus of the resected specimen showed the Rhinosporidium extending up to the cartilage. Local removal of the diseased area would not have been satisfactory. Surgical excision appears to have given us satisfactory results since there is no recurrence so far.

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EXPERIMENTAL SURGERY

THE RELATIVE IMPORTANCE OF THE STORAGE AND SECRETORY FUNCTIONS OF THE STOMACH IN THE MAINTENANCE OF NUTRITION IN THE RAT

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"*Some have made the stomach a mill; some would have it to be a stewing pot; and some a wort-trough; yet all the while, one would have thought it must have been very evident, that the stomach was neither a mill, nor a stewing pot, nor a wort-trough, nor any thing but a stomach.*"—WILLIAM HUNTER.

DISTURBANCES of nutrition and of alimentary function are common following gastrectomy in man and experimental animals. Loss of weight, anæmia, and impaired absorption of food have been investigated intensively, but their cause is not completely understood (Welbourn, 1953). It has become clear since William Hunter wrote the above words that the stomach has two main functions: it provides a reservoir for the storage, liquefaction, and mixing of food and it elaborates external and internal secretions. Much is known about these, but their relative importance in maintaining normal nutrition and alimentary function has not been determined.

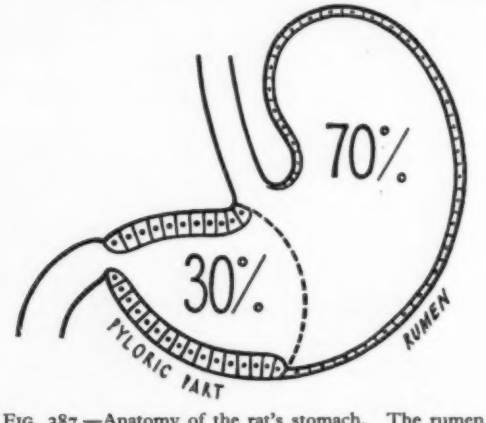

FIG. 387.—Anatomy of the rat's stomach. The rumen is lined by squamous epithelium and provides about 70 per cent of the capacity. The pyloric part is lined by secretory columnar epithelium and provides only 30 per cent of the capacity.

The problem can be conveniently studied in the rat for two reasons: first, in this species the two functions of the stomach are largely subserved by anatomically separate parts (*Fig.* 387). The rumen is lined by non-secretory squamous epithelium and provides up to 70 per cent of the storage capacity, while the pyloric part is lined by secretory columnar epithelium and provides only about 30 per cent. By removing these two portions separately and re-establishing the continuity of the gut, it is possible to distinguish between the effects of greatly reducing the capacity of the stomach and of eliminating its secretions. Secondly, total gastrectomy in the growing rat is regularly followed by severe hypochromic, microcytic anæmia and, after an interval of a few weeks during which the weight increases, by rapid loss of weight and death (Bussabarger and Jung, 1936; Balfour, Higgins, and Woods, 1950).

Attempts have been made to prevent the anæmia and loss of weight by varying the diet, by adding specific substances to it, or by giving them parenterally.

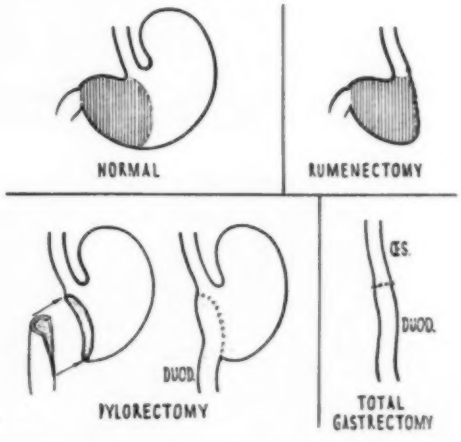

FIG. 388.—Operations performed on rats in first experiment.

The present investigation comprised three experiments in rats. The purpose of the first was to observe the effects of removing the whole stomach, and of removing its two parts separately, on (*a*) body-weight, (*b*) the blood-picture, (*c*) the consumption of food, and (*d*) the absorption of food. The purpose of the second and third was to observe the effects of giving various supplements, either orally or parenterally, to rats which had undergone total gastrectomy.

METHODS

In the first experiment 4 groups of female albino Wistar rats were used (*Fig.* 388):—

1. Control—7 rats underwent laparotomy only;
2. Rumenectomy—5 rats had the rumen only removed and the pyloric end of the stomach closed by a continuous invaginating suture;

3. Pylorectomy—5 rats had the pyloric end of the stomach removed and the duodenum sutured to the œsophagus and rumen by one layer of invaginating interrupted sutures;

4. Total gastrectomy—5 rats had the whole stomach removed and the duodenum sutured to the œsophagus by six or seven interrupted invaginating sutures.

All operations were done under light anæsthesia with antiseptic, but not aseptic, precautions. The suture material was 00000 Mersilk, threaded on fine corneal needles. The animals were deprived of food, but not water, from the evening before operation and were given 20 ml. of normal saline subcutaneously at the time of operation. For the first post-operative day they were given nothing by mouth, on the second day they were given half-normal saline, and from the third day onwards they were allowed normal food and tap water. The food was 'pig starter meal', supplied in cubes, a diet on which rats thrive in this laboratory. Eight other animals, which died from anastomotic leaks in the first week after operation, were not included in the study.

The rats were all about three months old and growing fast at the beginning of the experiment. Their initial weights varied from 116 to 154 g. and were similar in all four groups. They were weighed immediately before operation, daily until they had regained their initial weight, and weekly thereafter.

Blood examinations were made at intervals after operation. Samples of blood were taken under light ether anæsthesia by making a small longitudinal incision in the tip of the tail and allowing the blood to drip into a glass container where it was mixed with heparin. The hæmoglobin concentration was measured with a grey wedge photometer, red-cell counts were made, the P.C.V. was measured with a microhæmatocrit tube, and blood-films were stained and examined.

The amount of food which each animal ate at various times was determined by feeding a known quantity and weighing the residue after three days.

Fat and nitrogen intake and excretion studies were performed, once on all the rats and twice on most, by a method similar to that which had previously been used for dogs (Welbourn, Hallenbeck, and Bollman, 1953). The animals were placed in individual metabolic cages and fed on a high-fat (15–21 per cent) diet, consisting of pig starter meal and added lard, for five days. On the first and fifth days the diet was uncoloured. From the second to the fourth day a known weight of the diet, coloured with carmine (0·2 per cent), was given and the quantity that was eaten was determined by weighing the residue at the end of the period. The carmine-coloured fæces were collected and preserved in dilute hydrochloric acid.

Table I.—Length of Survival and Cause of Death in Rats in Experiment I

Group	Description	Rat No.	Length of Survival in Weeks	Cause of Death
1	Control	1	94+	(Living)
		2		
		3	68	Intercurrent disease
		4	94+	(Living)
		5		
		6		
		7		
2	Rumenectomy	1	98+	(Living)
		2	80	Intercurrent disease
		3	98+	(Living)
		4	24	Intestinal obstruction
		5	44	Anæsthetic accident
3	Pylorectomy	1	98+	(Living)
		2	32	Malnutrition
		3	48	
		4	48	
		5	12	
4	Total gastrectomy	1	21	Malnutrition
		2	26	
		3	24	
		4	15	
		5	15	

The fat content of the diet was estimated by an ether extraction method, and that of the fæces by the wet-extraction method of van de Kamer, Huinink, and Wyers (1949). The nitrogen in the diet was estimated by macro-Kjeldahl digestion and titration and that in the fæces by micro-Kjeldahl digestion, followed by measurement of the colour produced after the addition of Nessler's reagent.

In the second experiment 7 groups of male rats were used:

1. Control—2 rats underwent laparotomy only.
2. Total gastrectomy—2 rats.

The rest underwent total gastrectomy and were then fed various substances in the drinking water:

3. Neutralized human gastric juice, 5 ml. per day—2 rats.
4. Ferric ammonium citrate, 1 mg. per day—2 rats.
5. Gastric juice as in (3)+iron as in (4)—3 rats.
6. Vitamin B_{12}, 0·2 μg. + intrinsic factor, 1 mg. per day*—2 rats.

* The proprietary preparation "Biopar" (Armour Laboratories) was used.

7. Vitamin B_{12} and intrinsic factor as in (6) + iron as in (4)—2 rats.

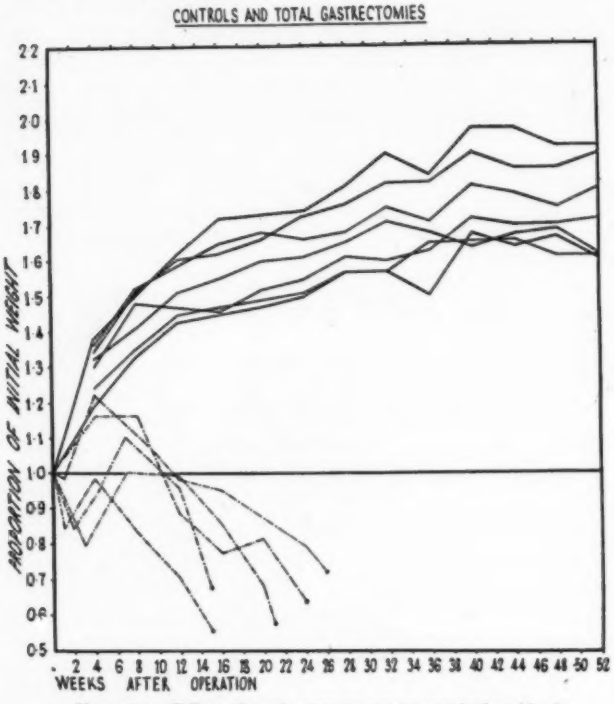

FIG. 389.—Effect of total gastrectomy on survival and body-weight. Solid lines indicate controls and broken lines total gastrectomy.

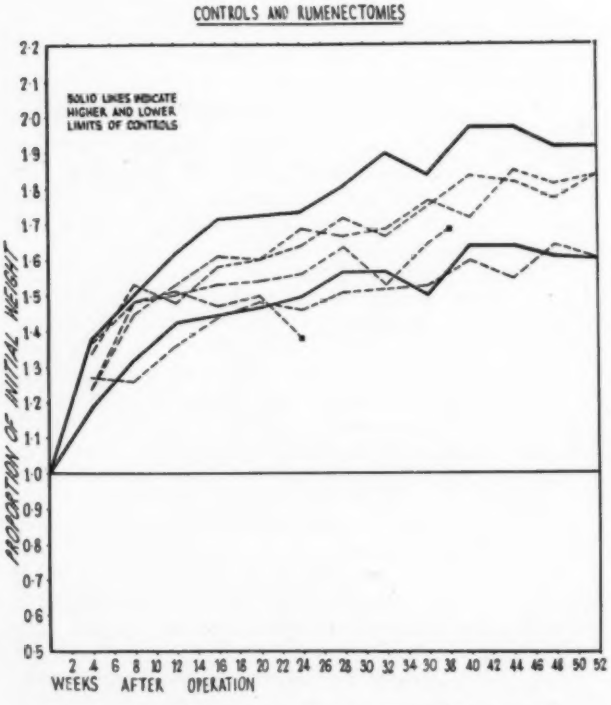
CONTROLS AND RUMENECTOMIES
SOLID LINES INDICATE HIGHER AND LOWER LIMITS OF CONTROLS
PROPORTION OF INITIAL WEIGHT
WEEKS AFTER OPERATION

FIG. 390.—Effect of rumenectomy on survival and body-weight.

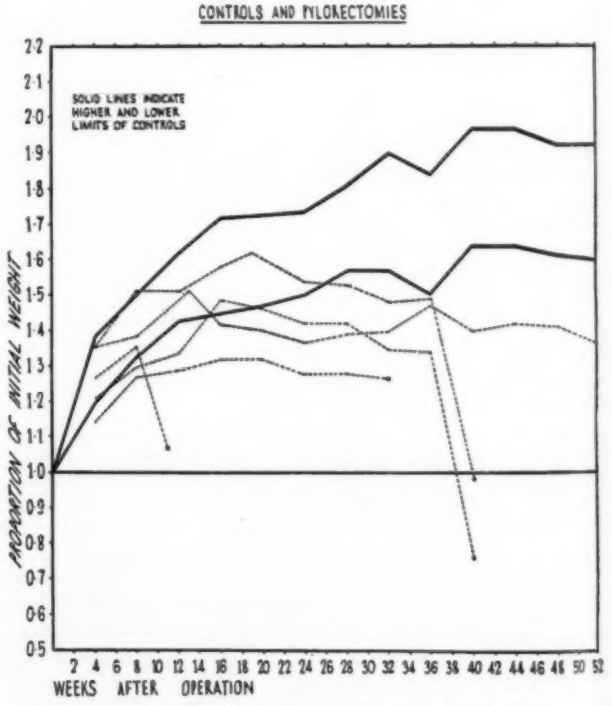
CONTROLS AND PYLORECTOMIES
SOLID LINES INDICATE HIGHER AND LOWER LIMITS OF CONTROLS
PROPORTION OF INITIAL WEIGHT
WEEKS AFTER OPERATION

FIG. 391.—Effect of pylorectomy on survival and body-weight.

Five other animals, which died under anæsthesia or from anastomotic leaks, were not included in the study. The neutralized human gastric juice was obtained by filtering pooled specimens from gruel fractional test-meals, all of which had initially contained free hydrochloric acid, and neutralizing them with normal sodium hydroxide. The juice was stored in a refrigerator at 0° C. The final concentration of sodium chloride in the drinking water was about 0·15 per cent. The animals were weighed regularly and blood samples were examined at intervals as in the first experiment.

In the third experiment one of the rats (in group 2 of the second experiment) which had undergone total gastrectomy and received no dietary supplement was used. When it was losing weight rapidly and was unlikely to survive much longer it was given fresh rats' stomachs, with their contained food, to eat. It received eleven stomachs in the first three weeks and one weekly thereafter. It was also given 5 mg. of iron (0·1 ml. of " Imferon " Benger, a dextran–iron complex) by intramuscular injection at intervals.

RESULTS

Experiment 1.—The animals took their food normally and thrived for varying periods after operation (*Table I*).

Body-weight.—The changes in body-weight during one year after operation are shown graphically (*Figs.* 389–391). For comparison all the weights have been calculated as a proportion of the pre-operative weight, which is shown as 1·00 for every animal. All lost weight immediately after operation, but all except those which had undergone total gastrectomy had regained their pre-operative weights within a week. The control animals (*Fig.* 389) gained weight rapidly for 4 to 5 weeks, and more slowly thereafter. After total gastrectomy (*Fig.* 389) the animals reached a peak at from 4 to 8 weeks after

operation and all but one rose above their initial weights. From then on their weights fell steadily until they died 15 to 26 weeks after operation. Rumenectomy (*Fig.* 391) had no effect on body-weight, and all the rats in this group, with the exception of the one that developed intestinal obstruction, behaved exactly like the controls. Pylorectomy

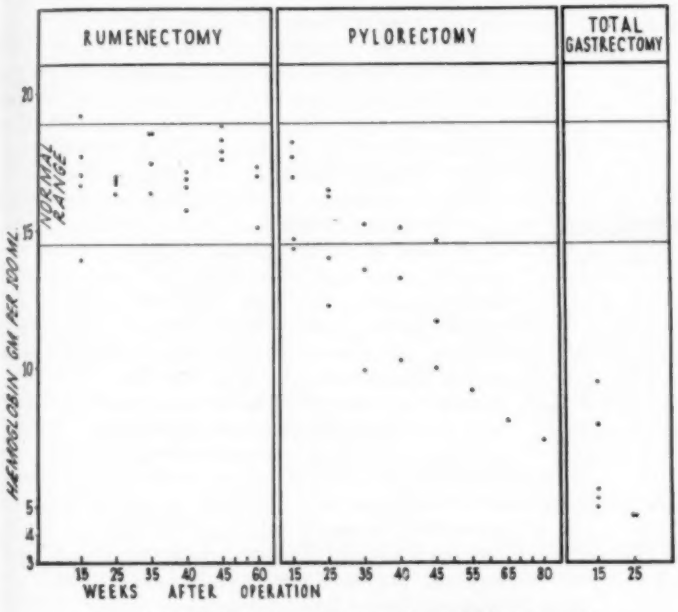

FIG. 392.—Effect of operations on hæmoglobin concentration. The normal range was obtained from the control group. Each point represents a single observation on one animal.

(*Fig.* 391), on the other hand, had a marked, but delayed, effect. After an initial gain in weight, similar to that seen in the control and rumenectomy groups, all the animals reached a peak at between 8 and 19 weeks after operation. The weight then fell, usually slowly at first and more rapidly later, until after 11 to 48 weeks 4 of the 5 had died. The fifth was still alive after 98 weeks, but was losing weight slowly and steadily.

Blood-picture (*Fig.* 392).—The control animals maintained a normal blood-picture throughout the experiment, their hæmoglobin concentrations varying between 14·5 and 18 g. per 100 ml. Rumenectomy had no significant effect. The pylorectomy group, however, slowly developed moderate anæmia, while the total gastrectomy group rapidly developed severe anæmia. The anæmia in all cases was of the microcytic, hypochromic type.

Consumption of Food (*Table II*).—The control animals and those which had undergone rumenectomy ate similar amounts of food throughout the experiment, and their consumption increased as their weights rose. Those in the pylorectomy group ate the same amount for the first few weeks, but later, when they were losing weight, were found to be eating slightly less. Their consumption fell sharply just before death. After total gastrectomy the intake of food was low from the beginning and fell lower still as weight was lost. All the animals ate far more food by night than they did by day.

Although food was sometimes present in the œsophagus, the gastric remnants and intestines of the animals which had died after losing weight were found empty at autopsy.

Absorption of Food.—Fat and nitrogen intake and excretion studies were made on all the animals at 8 to 14 weeks after operation and again on all surviving animals at 24 to 30 weeks. The control rats and those which had undergone rumenectomy

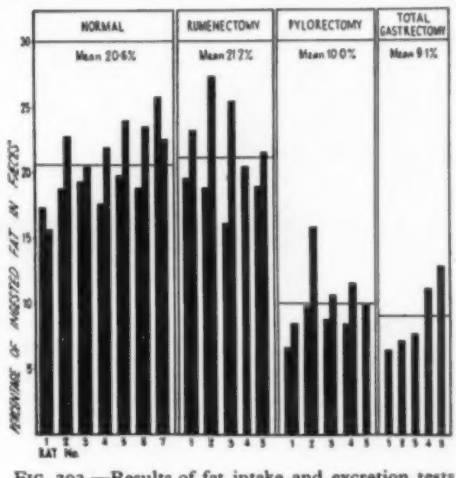

FIG. 393.—Results of fat intake and excretion tests. Each column represents one test.

excreted in the fæces about 20 per cent of the fat which they ate, while the pylorectomy and total gastrectomy groups excreted only about 10 per cent (*Fig.* 393). All the animals excreted about 30 to 40 per cent of the nitrogen which they consumed (*Table III*).

Experiment 2.—None of the substances which were given in the drinking water had any effect on the weights or blood-pictures of the rats, and all in groups 2–7 behaved in a similar manner to those which had undergone total gastrectomy in the first experiment. The control animals (group 1) gained weight normally and were killed after 31 weeks. The survival times of all the animals are shown in *Table IV*. Dilute neutralized gastric juice seemed to be abhorrent to the rats and those which were receiving it drank less fluid than the others.

Table II.—WEIGHTS OF FOOD EATEN BY DIFFERENT GROUPS OF RATS DURING TEST PERIODS

TIME AFTER OPERATION (WEEKS)	AVERAGE WEIGHT OF FOOD EATEN (g. per day)			
	Control	Rumen-ectomy	Pylor-ectomy	Total Gastrec-tomy
8–14	13·8	12·8	13·0	7·5
24–30	15·1	15·5	13·2	—
56–60	15·8	16·4	11·0*	—

* Only one surviving.

Experiment 3.—The rat which was used in this experiment (*Fig.* 394) had lost weight for 2 weeks, then gained it rapidly for 7 weeks, and had finally lost weight steadily for 17 weeks. Its hæmoglobin concentration had fallen to 5·9 g. per 100 ml.

When given whole rats' stomachs with their contained food it ate them ravenously. It started to eat more and to regain weight within a week of receiving the first stomach and regained in 25 days

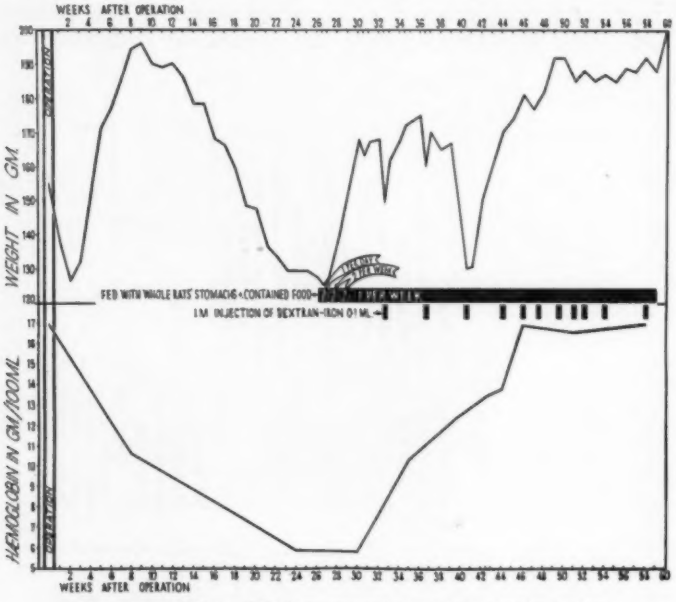
WEEKS AFTER OPERATION
WEIGHT IN GM.
HAEMOGLOBIN IN GM./100ML.
FED WITH WHOLE RATS' STOMACHS + CONTAINED FOOD
I.M. INJECTION OF DEXTRAN-IRON 0·1 ML.
WEEKS AFTER OPERATION

FIG. 394.—Effects of feeding stomachs and injecting iron after total gastrectomy in a rat.

more than half what it had lost. It then started to lose weight again (although it was still receiving a stomach every week) and was given sufficient iron intramuscularly (5 mg.) to restore its theoretical deficiency, calculated from the hæmoglobin concentration. It again gained weight for about 3 weeks, but then again started to lose. Twice more an injection of iron restored its weight, the effect of each injection lasting for about 3 weeks. On the fourth occasion iron was given when the weight appeared to be at its peak and this time there was no fall. Further regular injections increased the weight more and maintained it at about the optimal post-operative level. The hæmoglobin concentration remained constant when stomachs alone were given, but rose steadily with each injection of iron, reaching a normal level of 16·0 g. per 100 ml. 14 weeks after the first injection.

The animal remained in good condition 65 weeks after operation, by which time it had survived twice as long as any rat which had previously undergone total gastrectomy in this laboratory. It then lost weight rapidly and died 3 weeks later.

Table III.—EXCRETION OF NITROGEN IN THE FOUR GROUPS OF RATS

(The differences are not statistically significant)

GROUP	AVERAGE PROPORTION OF INGESTED NITROGEN EXCRETED IN FÆCES (PER CENT)	
	1st Test	2nd Test
Control	33·1	30·7
Rumenectomy	34·5	36·6
Pylorectomy	36·5	36·5
Total gastrectomy	37·0	—

DISCUSSION

The results indicate that removal of the main storage compartment of the rat's stomach (rumenectomy) has no effect on its ability to gain weight and maintain a normal blood-picture under laboratory conditions. Removal of the secretory portion alone (pylorectomy) or of the whole stomach (total gastrectomy), however, causes loss of weight, anæmia and death after varying periods. It would appear, therefore, that the secretory function of the stomach is more important than its storage function in maintaining normal nutrition. The fact that the effects of pylorectomy are less severe and more delayed than those of total gastrectomy indicates, however, that the storage function is of *some* importance.

There are three possible ways in which gastrectomy might cause loss of weight: first, the animals might eat too little food; secondly, they might fail to absorb what they did eat; and, thirdly, their metabolic rates might be increased. Our results show that there is a close correlation between the amount of food which is eaten and the gain or loss of weight. After rumenectomy there is no impairment of food intake or of body-weight; after total gastrectomy the intake of food is seriously impaired from the beginning; after pylorectomy it becomes impaired as the animals begin to lose weight, and after both total gastrectomy and pylorectomy the intake falls off markedly when weight loss is rapid just before death. Impaired absorption of food is clearly not a factor in causing the loss of weight, since the excretion of nitrogen in the fæces is not affected while that of fat is actually reduced by pylorectomy and by total gastrectomy. This observation is contrary to the usual finding in man and the dog, and there is no obvious explanation for it. It cannot be explained by differences in the quantity of food consumed, because the rumenectomy and pylorectomy groups were eating the

Table IV.—LENGTH OF SURVIVAL AFTER TOTAL GASTRECTOMY OF RATS IN EXPERIMENT 2

GROUP	DESCRIPTION	RAT NO.	LENGTH OF SURVIVAL IN WEEKS
1	Control	1 2	31 (killed) 31 (killed)
2	Total gastrectomy	1 2	11 26+
3	Total gastrectomy + gastric juice	1 2	10 17
4	Total gastrectomy + iron	1 2	23 26
5	Total gastrectomy + gastric juice + iron	1 2 3	14 16 24
6	Total gastrectomy + vitamin B_{12} and intrinsic factor	1 2	28 30
7	Total gastrectomy + vitamin B_{12} and intrinsic factor + iron	1 2	18 22

same amount at the time of the tests. No observations on metabolic rate were made.

The reduced intake of food could account largely, if not entirely, for the loss of weight which occurs some weeks or months after gastrectomy, and we must seek the cause of the animals eating less. It is not solely the result of an impaired capacity, since this would take effect immediately after operation. A possible cause is obstruction to the passage of food as a result of squamous hyperplasia in the œsophagus (Balfour, Higgins, and Woods, 1950) or rumen (Watson and Florey, 1955) which develops slowly after total gastrectomy or pylorectomy. Our own histological studies were unsatisfactory because the specimens were obtained some time after death, but marked hyperplasia was seen in one œsophagus.

The factors in the secretory portion of the stomach, whose absence causes nutritional impairment, have been studied by Balfour, Higgins and Woods (1950), who have found that they are able to prevent weight loss to some extent by the feeding of whole rats' stomachs, neutralized human gastric juice (by stomach tube), and iron. The results of our second experiment indicate that neutralized human gastric juice, vitamin B_{12}, intrinsic factor, and small doses of iron, *given in the drinking water* (and not by stomach tube), have no effect on body-weight or survival when given alone or in various combinations. Our third experiment confirms that there is some factor in the rat's stomach or its contents which restores body-weight, but that it only does so temporarily. The weight can be restored completely, and maintained, by giving iron intramuscularly in addition to stomach. It remains to be seen whether iron alone will have the same effect.

The anæmia could be caused by either a reduced intake or an impaired absorption of iron, or by both. It was already apparent in the pylorectomy and total gastrectomy groups 15 weeks after operation when the blood was first examined, and by this time the consumption of food was already falling. The anæmia was of the microcytic hypochromic type, which is always found after total gastrectomy in animals. This is interesting since total gastrectomy, which impairs the absorption of vitamin B_{12} in the rat (Watson and Florey, 1955; Nieweg, Arends, Mandema, and Castle, 1956) and in man (Callendar, Turnbull, and Wakisaka, 1954), frequently causes megaloblastic anæmia in human subjects (Welbourn, Nelson, and Zacharias, 1956). It has been stated in previous reports that the anæmia which follows total gastrectomy in the rat is only partly corrected by iron therapy and is not influenced by gastric juice, vitamin B_{12}, or folic acid (Bussabarger and Jung, 1936; Higgins, Ingle, and Joneson, 1947; Balfour, Higgins, and Woods, 1950). Our results show that small doses of ferric ammonium citrate by mouth have no effect but that iron, given intramuscularly (together with rats' stomachs by mouth) restores the blood to normal.

No conclusions which are of importance in human physiology or pathology can be drawn from these observations at present.

SUMMARY

1. The relative importance of the storage and secretory functions of the stomach in the maintenance of nutrition was studied in the rat.

2. Total gastrectomy, excision of the rumen (reservoir portion) only, and excision of the pyloric part (secretory portion) only, were performed in different groups of animals and their effects compared.

3. The body-weight and food consumption were measured and the blood-picture was examined at intervals, and fat and nitrogen intake and excretion studies were performed.

4. Total gastrectomy caused, after an interval of a few weeks, rapid loss of weight, severe iron-deficiency anæmia, and death. Rumenectomy had no effect. Pylorectomy had a similar effect, but considerably delayed, to that of total gastrectomy.

5. Food consumption fell as the animals lost weight.

6. Total gastrectomy and pylorectomy improved the absorption of fat, while rumenectomy did not affect it. The absorption of nitrogen was similar in all groups.

7. The addition to the drinking water of neutralized human gastric juice, small doses of iron, vitamin B_{12}, and intrinsic factor, alone and in various combinations, had no effect on rats after total gastrectomy.

8. The feeding of whole rats' stomachs plus their contents to one rat after total gastrectomy caused a striking but temporary increase in weight, but no change in the hæmoglobin concentration. The intramuscular injection of iron, in addition, caused complete restoration of the weight and blood-picture.

9. It is concluded that the secretory function is much more important than the reservoir function of the stomach in maintaining nutrition in the rat, and that iron is of great importance in the maintenance of body-weight as well as in hæmopoiesis.

We are grateful to Dr. M. G. Nelson, Dr. I. D. A. Johnston, and Mr. A. Lamont, F.I.M.L.T., for the blood examinations; Mr. K. L. Robinson of the Department of Agricultural Chemistry, Queen's University, for the diet analyses; and Messrs. G. A. Smith and R. G. Wood for the diagrams.

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SHORT NOTES OF RARE OR OBSCURE CASES

A ONE-STAGE NEPHRO-URETERO-CYSTECTOMY

By THOMAS MOORE, Manchester

Very radical surgery is now commonplace. It is, therefore, rather to emphasize some of the lessons it teaches than to demonstrate how radical a urological procedure can be successfully accomplished that this case is being reported in detail.

CASE REPORT

Mrs. I. M., aged 39. Transferred to my care by a colleague on April 24, 1949.

History.—Patient stated that she had been in hospital in April, 1946, having a child and that during this time had passed blood in the urine. Was strongly advised to have investigations but refused. Since, she has had hæmaturia on and off for a few days at a time. Has no pain on passing urine, just a slight stinging at the end.

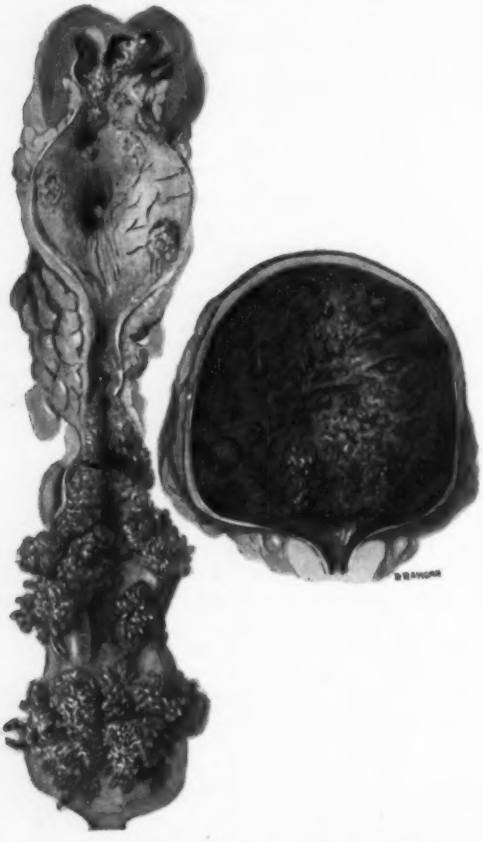

Fig. 395.—Coloured drawing of left kidney and ureter and bladder, showing diffuse papillary tumours.

Slight frequency of micturition and has to get up 1–3 times at night. For the last two days has complained of some pain in the left loin referred to the left groin. Otherwise well.

On Examination.—Patient very fat and in good condition.

Abdomen: Some tenderness left renal angle. Kidney not palpable.

P.R. and P.V.: N.A.D.

Other systems: N.A.D.

Investigations.—Urine: Microscopical: numerous R.B.C. Culture: *B. coli*. *Blood-count*: R.B.C. 3,900,000. Hb 44 per cent. W.B.C. 10,300.

Cystoscopy (Low spinal anæsthesia): Very extensive papilliferous growth involving practically the whole of the base of the bladder. Neither ureteric orifice was visible. There were numerous seedling deposits all over the dome of the bladder. On bimanual examination an ovarian cyst the size of a large orange could be felt. No induration of the bladder neoplasm was detected.

Plain radiograph of abdomen: No abnormality except that the soft-tissue shadow of the left kidney looked a little large.

Intravenous urogram: Good function on the right side but considerable dilatation of the ureter pelvis and calices. On the left side the function was very poor and no definite outline of the ureter could be seen. The cystogram showed a very gross filling defect in the bladder.

Blood-urea: 33 mg. per 100 c.c.

The patient was prepared for total cystectomy on orthodox lines.

At Operation (May 2).—Under general anæsthesia. Lower abdominal midline incision. Peritoneal cavity opened. There was a cyst arising from the left ovary about the size of a Jaffa orange; it was removed. The pelvic colon was reflected medially and the left ureter exposed. It was grossly enlarged and had a curious spongy soft feeling. It was realized that it was full of papillary growth. The wound was extended upwards and the left kidney exposed extraperitoneally. The pedicle was clamped and the kidney mobilized. The ureter was then mobilized right down to its junction with the bladder, where it was of normal calibre and appeared to be free from growth. This part was destroyed with diathermy and divided, both ends being ligated. The left kidney and ureter were removed. The right ureter was then exposed just below the pelvic brim. It was very dilated. It was divided about 2 in. from the bladder and the lower end tied. The upper end was transplanted into the right side of the pelvic colon by Coffey's method and the anastomosis was extraperitonealized. After this procedure the patient's condition was still good and the operation was continued and the bladder removed. The wound was closed in layers and the pelvic cavity was drained through a urethral catheter.

Progress.—The patient was somewhat shocked after the total cystectomy and required a blood transfusion of 3 pints before her general condition improved.

Afterwards, she made slow but steady progress, and was eventually discharged on June 3. At this time the wound was healed, although there was some weakness of the scar. Her hæmoglobin was 60 per cent. The blood-urea was 37 mg. per 100 c.c. Afterwards the patient enjoyed good health and carried out her normal household duties, although frequent checks of the blood-urea showed it to be raised to 60 mg. per 100 c.c. The intravenous urogram showed that there was still considerable dilatation of the right kidney and ureter.

On Jan. 3, 1951, the patient was re-admitted to hospital complaining of loss of weight and energy. On examination, she was obviously very ill and anæmic and abdominal examination showed gross liver enlargement with nodules palpable in it. In spite of blood transfusions and general treatment her condition showed little improvement. She was discharged home at her own request and died in February. No autopsy was possible.

PATHOLOGY REPORT.—*Specimen* 1: A unilocular, simple ovarian cyst the size of a Jaffa orange.

Specimen 2 (*Fig.* 395): Consists of bladder, left kidney, and ureter. The kidney measures 11 × 5 × 3·5 cm. On section there is a hydronephrosis with marked thickening of the wall of the pelvis which is studded with nodules of papillomatous growth. The calices are dilated and only a narrow rim of kidney tissue remains. The whole length of the ureter is dilated, measuring 3 cm. in diameter. The wall is thin. Papillomatous tissue is arising from the lining along the whole course of the ureter and filling the lumen. The growth is closely packed at the lower end of the ureter. The bladder has been opened and measures approximately 10 cm. in diameter. The wall is thin, but arising from almost the whole of the mucosa are low, shaggy papillomatous structures. Blood-clot mixed with tumour tissue is present in the bladder.

Microscopical: Sections of bladder and ureter show multiple villous structures with a central core containing blood-vessels covered by an orderly and typical transitional epithelium (*Figs.* 396, 397). The growth throughout is confined to the lining and does not extend downwards into the underlying structures of the wall. Sections of the kidney show similar but less luxuriant villous structures arising from various parts of the lining of the pelvis but no extension into deeper tissues. There is marked hydronephrosis and dilatation of the calices. The renal parenchyma is infected, many of the tubules containing pyogenic exudate. The glomeruli show thickening of the capsules, periglomerular fibrosis or infiltration with chronic inflammatory cells mixed with leucocytes. In some areas the tubules are compressed and atrophic or replaced by fibrous tissue. Histologically, the appearances are those of multiple papilloma of the bladder, ureter, and renal pelvis, with a recurrent pyelonephritis. In view of the marked hydronephrosis it would seem likely that the original growth occurred in the bladder near the ureteric orifice or lower end of the ureter, although it is recognized that multiplicity of tumours in the urinary tract has been attributed to multi-focal tumour formation rather than implantation metastases.

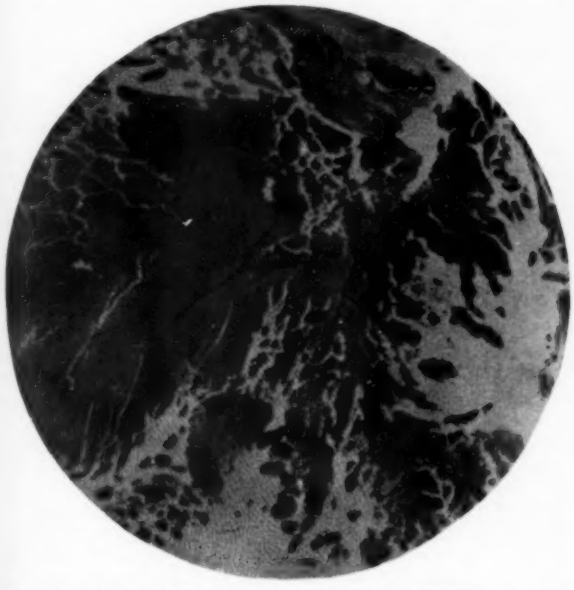

FIG. 396.—Photomicrograph of part of ureteric tumour. (× 7·5.)

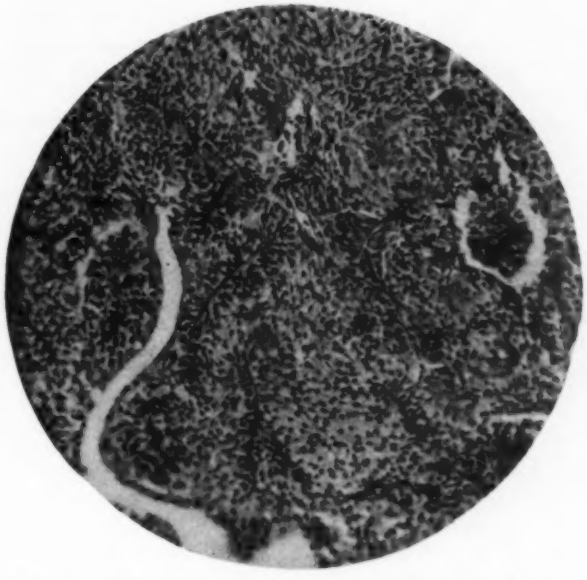

FIG. 397.—Photomicrograph of part of ureteric tumour. (× 52·5.)

DISCUSSION

That the left ureter was full of neoplasm was not discovered pre-operatively in this case. This is a common occurrence in advanced cases of papilliferous bladder tumours. One or both ureters may be obstructed so that renal function is too poor to allow of ureteric visualization by intravenous urography. At the same time one or both orifices may not be visible cystoscopically, so retrograde pyelography is not possible. The only method of finding out the state of the ureter is by surgical exploration, when one must be prepared to remove the involved ureter and its attached kidney. One must not fall into the trap in these cases of treating the bladder alone, either by surgery, radiotherapy, or a combination of both. When the ureter and kidney have been dealt with the bladder should then be treated by the most suitable method, either at the same time or later.

In this case the tumours histologically were believed to be simple, but of course it was impossible to examine all the innumerable tumours present. Clinically some of them undoubtedly were malignant and led eventually to metastases. It is well recognized that ureteric neoplasms which are histologically benign are often clinically malignant. It was disappointing that the patient only lived for eighteen months after the operation, but for the greater part of this time she was carrying out her normal household duties and was clinically perfectly well. It is unlikely that any other type of therapy could have cured her or given her an equally long period of comfortable living.

I should like to acknowledge my indebtedness to Dr. Lois Stent for her help with the pathology in this case and to Miss D. Davison for the coloured drawing.

SPONTANEOUS RUPTURE OF THE BLADDER

By G. K. THOMAS

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SPONTANEOUS rupture of the bladder is a very rare catastrophe. Stone (1931) collected 40 cases from the literature between 1279 and 1929, assessed 37 as true cases and added 2 of his own. Crastnopol, Artz, and Rosett (1950) collected a further 19 more recent cases and added 4 cases of recurrent spontaneous rupture, which is even more rare. Bacon (1943) reviewed 147 cases of rupture of the bladder; of those, 102 were due to external trauma, 40 complicated transurethral instrumentation, and only 5 were spontaneous.

Aetiology.—Spontaneous rupture of the bladder is usually a sequel of :—

1. *Lesion in Bladder Wall.*—

a. Acute inflammation or ulceration, e.g., Stone's (1931) first case; Russell Taylor's (1948) case.

b. Chronic inflammation, e.g., tuberculosis (Moroney, 1943).

c. Malignant infiltration, e.g., 4 of Bacon's (1943) cases.

2. *Lesion at Bladder Outlet leading to Overdistension.*—

a. Calculus. Possible example, Stone's (1931) second case.

b. Blockage of bladder neck by a papilloma, e.g., Macalister's (1955) first case.

c. Prostatic obstruction, e.g., case here reported.

d. Urethral obstruction.

e. In the female, due to uterine or adnexal disease; or during labour.

It may, however, be *idiopathic*—that is, no preceding trauma and no lesion in the bladder or distal to it. Barnes and Steele (1935) recorded a case of rupture of an apparently normal bladder with no underlying pathology and without even a history of possible overdistension. Hershman and Allen (1954) describe their case of a negro who had an idiopathic spontaneous rupture; although the patient had a positive cerebrospinal fluid Hinton test, and fixed pupils, the authors deny a neurogenic bladder on cystoscopic and cystometric findings. Dixon and Strohl (1936) reported a case in a man undergoing treatment for syphilis. The rupture was idiopathic, but the authors thought there might have been a connexion with the luetic condition in spite of a normal central nervous system on examination. "Neurogenic dysfunction is a rare cause unless one classifies alcoholism in this category" (Macalister, 1955). Usually, overdistension precedes rupture (Jones, 1934) and particularly if the patient has had an excessive alcohol intake (Lipow and Vogel, 1942; Feigal and Polzak, 1946; Nemser and Weinberger, 1952; Clinton-Thomas, 1955). Hershman and Allen (1954) mention alcohol depression of the sensorium as a predisposition to rupture in an overdistended but otherwise normal bladder; this could well account for the several cases on record which have followed an alcoholic excess. Idiopathic spontaneous rupture can occur in a woman (Beresford-Jones, 1941).

Spontaneous rupture may be precipitated by a sudden increase in intra-abdominal pressure—attempted micturition, straining at stool, sudden lifting of a heavy weight, or during labour (Stone, 1931); or possibly by severe retching (Hershman and Allen, 1954). Macalister (1955) reports a case in a man of 51 years straining to void a post-operative retention of urine, and partly blames the direct stimulant effect of carbachol.

CASE REPORT

Mr. R. E. S., a retired engineer aged 76 years, was admitted on June 6, 1956 with a diagnosis of strangulated inguinal hernia. The patient gave a very poor history owing partly to a degree of senility and partly, no doubt, to the confusion brought on by his severe illness. He lived in London and three days previously had been motored down to Southend for his holidays. The journey was uneventful and the following day he had gone for walks, etc. The day prior to admission he was having his midday meal when a painful desire to micturate put him off his food. He rested and the pain practically went. He could only pass a little urine at a time. That evening he had a small frothy vomit. On the day of admission he complained of some abdominal pain, he had two small vomits, and he could not micturate voluntarily, though he passed some urine involuntarily twice, wetting his clothes. He had not noticed hæmaturia. He told the house-surgeon that in the recent past he had had some difficulty on micturition with nocturia up to seven times, but told me that he had had no trouble at all, only occasionally getting up once at night. His bowels usually emptied twice daily, but had not emptied that day; he thought he may have passed flatus. He was emphatic that he had had no injury; this was subsequenly confirmed by his landlady. He had not taken alcohol.

Past History: Pneumonia in his twenties; operations for cataracts eighteen and seventeen years ago; right inguinal herniorraphy two years ago; "a little indigestion" for some time.

ON EXAMINATION.—Pulse 88, regular. Temperature 98° F. Respirations 22. He was thin, feeble, and somewhat shocked, with mucosal pallor and coated tongue. In spite of this, he did not appear particularly dehydrated. His heart was normal to examination and there was no increase of venous pressure. Blood-pressure 170/90. His lungs expanded poorly, especially at the bases, where there were some crepitations, but were otherwise normal to examination, as was his central nervous system. Abdominally, he was a little distended, rigid, and very tender, with rebound tenderness. No mass or viscus was palpable, but there was a little dullness suprapubically. Some free intraperitoneal fluid was detected but no free gas. The abdomen was silent on auscultation. He had a recurrent right direct inguinal hernia, easily reducible, and a fatty epigastric hernia. Rectal examination: ballooning of the rectum, a firm rather irregular enlargement of his prostate, and ulcerated prolapsed piles. Hæmoglobin 12·7 g. per cent (86 per cent); blood-urea 70 mg. per cent.

The diagnosis was peritonitis due to perforation of a viscus; in view of the severity of the condition and as dehydration was minimal, operation was planned for two hours after admission. In the meantime, a Ryle's duodenal tube was introduced via a nostril and the patient was prepared and premedicated.

AT OPERATION.—Under general anæsthesia—thiopentone, nitrous oxide and oxygen, suxamethonium drip—and through a right lower rectus-displacing paramedian incision, 2 pints (1·14 l.) of free, amber-coloured fluid was sucked out of the peritoneal cavity. There was no reaction in the visceral or parietal peritoneum. The bladder was found to be the viscus ruptured; it had a wall about ⅛ in. (0·85 cm.) thick, with a perforation, large enough to admit three finger-tips, on the posterosuperior aspect of its fundus and slightly to the right. A little less than 1 pint (0·57 l.) of similar fluid remained in, and was aspirated from, the bladder. Through this hole one could inspect the bladder—there was no tumour, stone, or diverticulum. Trabeculation was present but slight. An enlarged, firm prostate could be seen and felt; there was some intravesical projection. There was no bleeding from the edge of the perforation and absolutely minimal ecchymosis into the edge, which was of uniform thickness. There was nothing to suggest a pre-existing lesion, such as solitary diverticulum or ulcer, at the site of the rupture.

What appeared to be the easiest procedure was then carried out—the intestines were packed off upwards, the defect in the bladder was enlarged slightly, and a trans-peritoneal, transvesical prostatectomy was performed by the Wilson Hey method. Good hæmostasis was obtained with diathermy, a 30 c.c.-bag Foley urethral catheter left in position, and the bladder defect together with its overlying peritoneum closed with two layers of chromic catgut. A drain from the rectovesical pouch was brought out via a suprapubic stab, and the abdominal wall was closed in layers. Operative blood-loss was 15 oz. (420 c.c.); this was covered by the transfusion of 1 pint (0·57 l.) of blood during the operation, followed by *N*/5 saline in 4·3 per cent dextrose until the next day, when the patient's oral fluid intake was satisfactory.

PROGRESS.—Post-operatively the patient had a 5-day course of streptomycin followed by a 5-day course of chloramphenicol. Convalescence was uneventful apart from a slight coliform infection in part of his wound, which soon subsided. The urethral catheter was removed on the eighth morning; the patient then rapidly resumed normal micturition.

HISTOLOGICAL REPORT.—"Prostatic tissue weighing 40 g.

"*Microscopy*.—Much of the tissue sectioned shows benign myoadenomatous hyperplasia, but one large area present is the seat of a rather poorly differentiated adenocarcinoma."

On discharge June 23 (seventeen days after admission) the patient was remarkably well. He was then on mandelamine tablets and he had been started on a permanent course of œstrogen. His blood-urea was 40 mg. per cent, serum acid phosphatase 0·5 K.A. units, and hæmoglobin 10·4 g. per cent (70 per cent). He was passing water perfectly normally, and was symptom-free.

Follow-up arrangements were made with his doctor in London.

DISCUSSION

Sites of Spontaneous Rupture.—

1. *Intraperitoneal*.—The posterosuperior peritonealized segment of the bladder usually ruptures, for the reasons given by Stone (1931) and Macalister (1955)—no support from bony pelvis and pelvic muscles; no anchoring by prostate and ligaments such as are present at the base; no support from anterior abdominal wall; weakest part developmentally.

2. *Extraperitoneal*.—The site of rupture is usually dependent upon the site of a bladder lesion (one of Stone's cases). If it is due to obstruction, the site is medial and posterior to a ureteric orifice, which is a weak part developmentally (Stone, 1931).

3. Combined intraperitoneal and extraperitoneal.

Signs and Symptoms.—Intraperitoneal rupture classically gives a sudden lower abdominal pain, with inability to pass urine or else the patient can pass only a little blood-stained urine. There may be nausea or vomiting. The signs are those of peritoneal irritation or peritonitis; free fluid may be detected; usually, no bladder distension is found. Shock may be gross or slight.

In extraperitoneal rupture the onset is usually insidious (Stone, 1931). Later "the patient experiences severe lower abdominal pain which may radiate to the back, thighs, perineum, and penis. There is an urgent desire to micturate, with inability to do so except in the cases of small ruptures, when a little blood-stained urine may be passed" (Pyrah, 1948). Signs include localized tenderness and rigidity suprapubically, with a palpable induration in this region later. There may be a boggy swelling palpable rectally in the tissues between the rectum and base of bladder. Later, pelvic and retroperitoneal cellulitis set in.

Investigations and Treatment.—The various authors have employed catheterization with instillation of a measured quantity of water and subsequent withdrawal, excretion pyelography, cystoscopy, catheteric or cystoscopic introduction of air followed by abdominal radiography, cystography, and, lastly, diagnostic abdominal paracentesis. Some of these tests are not safe (Gordon-Taylor, 1953) and many are uninformative in particular cases. If a case of intraperitoneal rupture presents, the abdominal findings justify prompt laparotomy, especially as the condition of the patient is likely to deteriorate. The peritoneal cavity can be sucked dry, the rent in the bladder repaired, and any cause for the preceding overdistension dealt with or noted for later operation. As regards bladder drainage, most authors (Macalister, 1955; Clinton-Thomas, 1955) say suprapubic cystostomy is essential, but if the rent can be easily closed (site accessible, thick bladder wall) and if the cause for the retention has been dealt with, as in the case reported here, perurethral drainage has been shown to be feasible.

In extraperitoneal rupture, cystoscopy is indicated and is not harmful (Stone, 1931). In Stone's first case urethral dilatation by the cystoscope was sufficient to allow micturition to be resumed and a spontaneous cure to take place. Any underlying bladder or other lesion should be treated at the time, or later, depending on its nature. More often than not, operation is called for when the diagnosis is made, and at operation not only should the bladder be drained but also careful attention should be paid to drainage of the perivesical tissues.

Mortality.—Stone (1931) gives the mortality as 92·3 per cent for intraperitoneal rupture, and 50 per cent for extraperitoneal rupture, on review of the 19 cases he collected prior to 1900. Between 1900 and 1929 (18 cases) the mortality for intraperitoneal rupture was 45·4 per cent, whilst that for extraperitoneal rupture was nil. In Bacon's (1943) series of 147 cases, which included traumatic ruptures, the total mortality was 44·2 per cent. Out of 5 case reports published since 1952, 3 cases have recovered.

The better prognosis in cases of extraperitoneal rupture is due to a greater possibility of spontaneous recovery (Zuckerkandl, quoted by Thomson-Walker, 1914; Mitchell, 1898).

The mortality figures are improved if the urine is sterile at the time of the rupture, if surgery is prompt, and if suitable antibiotics and intravenous fluids are given.

SUMMARY

1. A case of spontaneous intraperitoneal rupture of the bladder is reported. The preceding overdistension of the bladder was due to obstruction by the prostate gland, which contained a large area of carcinoma. There was no apparent precipitating cause for the rupture.

2. Unusual features in the reported case were the absence of a sudden episode in the history, the apparent absence of hæmaturia, the absence of bleeding at the time of operation, and the performance of a transperitoneal prostatectomy (which proved a very easy operation). Carcinomatous enlargement of the prostate appears to be unusual in this type of case.

3. The literature is reviewed.

4. Prompt surgery is advocated and the treatment of the case is described. It has been shown that suprapubic cystostomy is not essential for all cases.

Acknowledgements.—I thank Mr. Bernard J. Sanger for permission to operate on and publish this case and also for his advice on the proofs. I thank Miss A. Elsdale for obtaining good anæsthesia, Dr. H. Williams for the histological report, and Mr. P. W. Perryman for the biochemical investigations.

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PAGET'S DISEASE OF THE MALE BREAST

WITH REPORT OF A CASE ACCOMPANYING CARCINOMA OF BREAST WITH METASTASES TO BONES AND PITUITARY

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CARCINOMA of the male breast is a relatively infrequent finding and Paget's disease is quite rare. It is said to have been first described by John of Arderne in the fourteenth century. In extensive lists of cases of Paget's disease recorded by Cheatle and Cutler (1931), Inglis (1936), Muir (1927, 1931), Willis (1953), and Geschickter (1945) no example occurring in the male is included. Treves (1954) has briefly reviewed this subject and has added 2 to the 9 acceptable cases previously recorded in the literature. Treves in his review cites 5 instances of this disease enumerated by Sarason and Prior (1952) in an excellent survey, including 1 case described by them, but adds also 3 cases annotated by Deaver and McFarland (1917)—namely those described by Gintrac in 1856, Forrest in 1880, and Gaucher and Bricout in 1912. The 4 reports cited by Sarason and Prior are those of Archibald (1922), Elbogen (1908), Rubenstein (1930), and Sekiguchi. (1917). Jonas in 1910 reported an alleged instance of bilateral Paget's disease, but no histological examination of the skin is recorded and this cannot be accepted as proven. Sachs (1941) collected by questionnaire and search of the literature 178 proven carcinomas of the male breast, and of these only 2 showed Paget's disease, i.e., an incidence of 1·1 per cent, and cited Wainwright (1927) and Gilbert (1933) as recording no example of Paget's disease in two series of 78 and 47 carcinomas of the male breast. At Memorial Center, New York, there were recorded in twenty-seven years 131 cancers of the male breast, and of these only 2, those reported by Treves, showed Paget's disease, i.e., an incidence of 1·5 per cent.

In the Western Infirmary, Glasgow, in the years 1948–9 there were examined 242 carcinomas of the female breast and of these only 2 showed overt Paget's disease—an incidence of about 0·8 per cent, but as detailed examination was not invariably carried out this is probably an underestimate.

Carcinoma of the breast is now described in a 66-year-old male with Paget's disease of nipple and metastases to bone, skin, and pituitary gland.

CASE REPORT

The patient, a 66-year-old watchman, was admitted to Mr. Barnes's wards at the Western Infirmary, Glasgow, on Aug. 15, 1953, with a pathological fracture of the left femur.

There were nodules in skin and a palpable discoid mass in the left breast measuring 2·0 cm. in diameter, but no eczema or ulceration of the nipple was noted. Radiological examination showed osteolytic lesions in the shaft of the left femur.

Secondaries were demonstrated radiologically in pelvis, ribs, vertebræ, and skull. Biopsy of a skin nodule on Nov. 28, 1953, was reported by Dr. M. E. Catto as

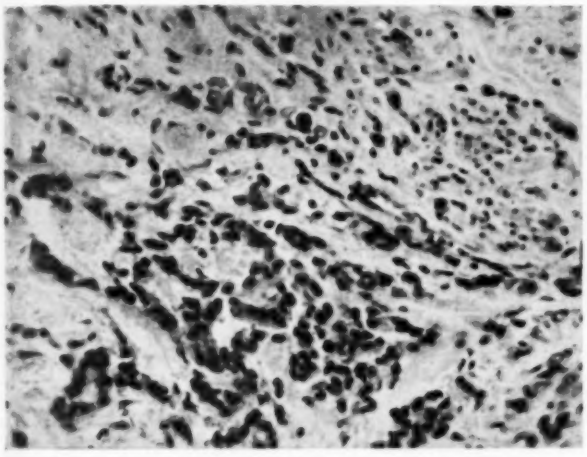

FIG. 398.—Typical spheroidal-cell carcinoma infiltrating through breast and eliciting a scirrhous reaction. Hæmalum and eosin. (× 210.)

FIG. 400.—Epidermis of nipple showing extensive infiltration by large pale Paget cells. H. and E. (× 82·5.)

a secondary carcinoma, probably with primary in the breast. The patient's condition gradually deteriorated and he died on Feb. 18, 1954.

Autopsy by Dr. W. A. Taylor on this emaciated old man showed a hard mass 2·0 cm. in diameter lying deep to and inferior to the left nipple, which was not macroscopically ulcerated. The right breast appeared normal.

Dissection revealed brown atrophy of the heart, and small nodules of secondary tumour in pleura and parenchyma of the lungs, which were emphysematous.

The bronchi, peritoneum, stomach, intestines, gall-bladder, liver, pancreas, adrenals, kidneys, prostate, and brain were free from primary tumour.

Section of the left breast showed scirrhous carcinoma. The axillary nodes were small, and not obviously invaded.

In the left femur there was an ununited spiral fracture in the upper part of the shaft, with the head and neck replaced by tumour within the hard bone and nodules also present in the marrow extending as far as the lower end. The lumbar vertebræ were densely sclerosed and the calvarium appeared normal.

HISTOLOGICAL EXAMINATION (A. T. S.).—

Right breast shows a small node of dense fibrous stroma through which are scattered occasional entirely normal ducts.

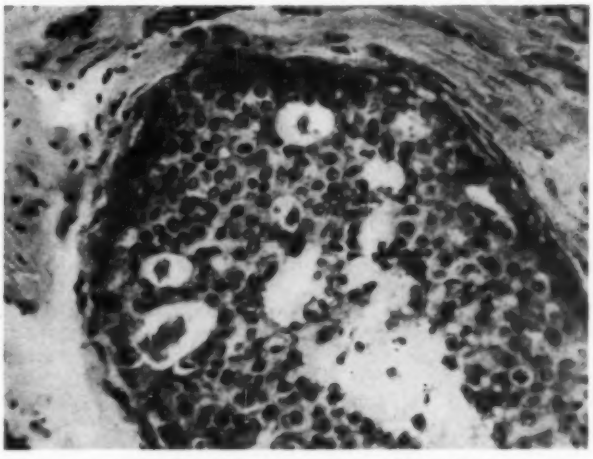

FIG. 399.—Cribriform intraduct carcinoma in depth of tumour. H. and E. (× 210.)

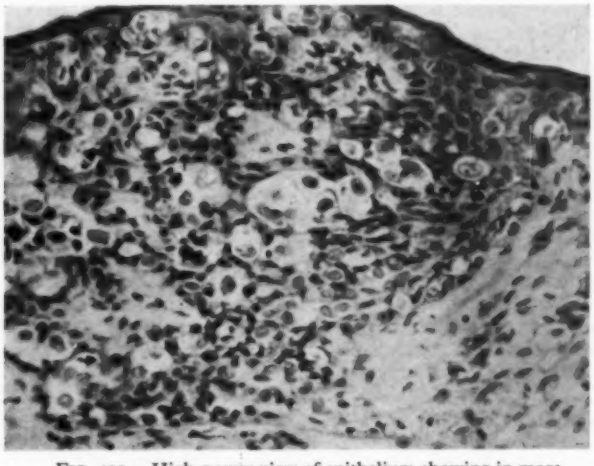

FIG. 401.—High-power view of epithelium showing in more detail the very marked infiltration of the nipple epidermis by typical Paget cells. H. and E. (× 210.)

Left breast: The breast tissue is replaced by a mass of fairly cellular spheroidal-cell carcinoma, largely in infiltrating cords eliciting a mild scirrhous reaction (*Fig.* 398). In other areas there is an acinar pattern. The tumour extends down to, but does not invade, the pectoral muscle. Perineural lymphatic dissemination is noted and the tumour also infiltrates upward through the cutis close to the overlying epidermis. Intraduct carcinoma with cribriform arrangement and central necrosis is apparent notably in the depths of the tumour (*Fig.* 399). Continuity between intraduct carcinoma and the Paget's disease in the epidermis was not confirmed, but this is probably explicable on technical grounds. Since Paget's disease was not suspected clinically or at autopsy the breasts were examined by the routine method used in a long-term investigation on breast structure in progress in this department. This requires section at right angles to the skin surface through the depth of the breast across the centre of the nipple and gives a maximal area of breast

tissue for study. In this instance the affected ducts were probably fairly centrally placed and may well have been removed by the technician paring into the blocks to obtain full-face sections. Weigert's stain for elastica reveals some evidence of obliterative change in a duct, the seat of intraductal neoplasia. Some hæmosiderin-containing macrophages are present throughout the tumour mass.

The epidermis of nipple and areola over a considerable area shows the changes of Paget's disease (*Figs.* 400, 401). The rete pegs are frequently widened and moderately deep. A round-cell infiltrate of not very severe degree is elicited in the cutis. The Paget cells occur singly and also in clumps of variable size. Nowhere is the basal layer completely replaced and the impression is one of an infiltrative process. The cells are moderately large and vary somewhat in size and shape, although the majority are ovoid. The cytoplasm is pale, watery, and faintly eosinophilic, sometimes appearing slightly granular. The cell membranes are well defined. The nuclei are vesicular and occasionally the nucleolus is eosinophilic and prominent. Occasional mitoses are seen. The Paget cells tend to group together towards the basal layers of the epidermis, but occasionally approach the squamous surface. Patchy hyperkeratosis is seen, but ulceration is not a feature. A significant proportion of the cells shows regressive changes with cytoplasmic condensation and nuclear pyknosis. In one limited area melanin-containing cells are present in the cutis, admixed frequently with round cells. This is confirmed by Fontana's stain, which shows also that the epidermis also contains melanoblast cells varying in number from field to field. Occasionally the Paget cells appear to contain very small quantities of melanin, but no melanin is present in the cells of the underlying carcinoma. Reference to the contralateral breast shows quite considerable pigmentation of the epidermis, especially marked in the basal layer, but no melanin is seen in the cutis. The appearances would appear to suggest that the infiltration by neoplastic cells has stimulated the melanoblasts in the affected nipple to the production of an excess of melanin, some of which is stored by melanophores in the cutis. It is now believed that melanin is formed by the dendritic melanoblasts and conveyed by them to the basal layer of the epidermis. In this instance it would appear that melanin has also been transferred from the dendritic cells to occasional Paget cells in the epidermis.

Pituitary: Shows small areas of old scarring in pars anterior. Spheroidal-cell scirrhous carcinoma is present in the capsule and in pars nervosa.

Prostate: Shows no evidence of carcinoma, but benign nodular hyperplasia of largely glandular type is present.

Lung: Reveals extensive dissemination by lymphatics of spheroidal-cell carcinoma.

Bone: Secondary neoplasm is seen in the left femur.

DISCUSSION

Much has been written on Paget's disease since the condition was described by Sir James Paget (1874). This marked the beginning of a long controversy on the essential nature of this disease. For an authoritative account of the pathology of Paget's disease reference may be made to Muir (1927, 1931). Briefly, Muir believes that continuity can usually be traced between the cells of the associated intraduct carcinoma and those infiltrating the epidermis. With this view Inglis (1936, 1946) is in full agreement. Other authors, e.g., Cheatle and Cutler (1931) and more recently Willis (1953), believe that Paget's disease is a primary epidermal change with concomitant change in the duct epithelium. Willis states that Paget's disease is a form of epidermal carcinoma in situ and identifies it with Bowen's disease. This view is rejected by Inglis (1946) and by most pathologists who have made a close study of these conditions.

The recorded cases show considerable variation in the age of incidence. Our patient was 66, that of Gaucher and Bricout (1912) (cited by Treves, 1954) 47, that of Sarason and Prior (1952) 55, and the two cases of Treves (1954) 67 and 80 years. In the patient of Gaucher and Bricout there was an alleged abnormality of the underlying breast since the age of 20, with redness of the nipple for five years preceding the disease. It is possible that in this instance some hyperplastic change in the breast may have preceded neoplasia. The duration of history in the present case is uncertain, but in that of Sarason and Prior was one year, and in those of Treves two months and eight months respectively. It is interesting to note that the two cases of Treves were the only ones diagnosed clinically.

It is of interest also that in this case metastasis of the tumour to the pars nervosa of the pituitary gland occurred. In our experience cases of mammary carcinoma coming to autopsy not infrequently show this finding, and probably are second only to those of bronchial carcinoma in the frequency with which they show metastasis to the pituitary. Willis (1952), in his monograph on the spread of tumours, points out that metastasis by mammary carcinoma is common to the pars nervosa, the pars anterior being rarely affected.

SUMMARY

Paget's disease of the male breast is a rare condition. Probably not more than 11 acceptable cases are recorded. The incidence of Paget's disease in carcinoma of the male breast does not differ grossly from that in the female, and only the relative infrequency of carcinoma of the breast in the male accounts for the considerable rarity of Paget's disease in this sex.

The views regarding the development of Paget's disease are briefly summarized and those of Muir are accepted as representing the true histogenesis.

A case of carcinoma of the breast in a man aged 66 is presented in which Paget's disease of the nipple was present and in which metastasis to the pituitary gland also occurred.

I am grateful to Mr. Roland Barnes for permission to publish this case; to Messrs. L. Nicolson and W. Mason for technical assistance; and to Professor D. F. Cappell for advice and encouragement.

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REVIEWS AND NOTICES OF BOOKS

Radiology of the Alimentary Tract in Infancy. By ROY ASTLEY, M.B., M.R.C.S., D.M.R., Radiologist, The Children's Hospital, Birmingham (United Birmingham Hospitals); Clinical Lecturer in Radiology and Lecturer in Radiological Anatomy, University of Birmingham. 9 × 5⅞ in. Pp. 287 + viii. Illustrated. 1956. London: Edward Arnold (Publishers) Ltd. 50s.

THERE can be little doubt that during the last decade the radiology of the alimentary tract in infancy has come into its own, and furnished important data to the surgeon.

In this monograph, which is well illustrated, Dr. Astley has given an interesting and very practical account of the various conditions, such as œsophageal atresia, vascular compression of the œsophagus, duplication of the foregut, diaphragmatic hernia, pyloric stenosis, duodenal obstruction, annular pancreas, and megacolon.

The radiographs, which are numerous, are all of good quality and demonstrate the clinical condition very well.

To-day many conditions found in infancy can be cured by surgery and the mortality-rate is small. The diagnosis of many of these conditions is confirmed by modern radiographic methods. Dr. Astley has demonstrated these methods in a very interesting way in this book.

Atlas of Exfoliative Cytology. By GEORGE N. PAPANICOLAOU, M.D., Ph.D. Supplement 1, 16 plates. 1956. Published for the Commonwealth Fund by Harvard University Press, Cambridge, Mass. (London: Cambridge.)

THIS atlas contains some of the most beautiful photomicrographs in colour that we have ever seen. The definition of the cell outlines and the nuclei and intracellular contents are excellent.

There can be little doubt that exfoliative cytology is an important branch of pathology and one in which British pathologists are taking an important part.

This atlas should find a place in every pathological department throughout the world.

Borderlands of the Normal and Early Pathologic in Skeletal Roentgenology. By DR. ALBAN KÖHLER. Tenth edition, completely revised by Doz. Dr. E. A. ZIMMER, Bern/Fribourg. English Translation arranged and edited by JAMES T. CASE, M.D., D.M.R.E. (Camb.), Professor Emeritus of Radiology, Northwestern University Medical School, Chicago; Director, Memorial Cancer Foundation, Santa Barbara, California. 10¼ × 6½ in. Pp. 723 + xvi, with 1300 illustrations. 1956. New York and London: Grune & Stratton Inc. $24.50.

THE tenth edition of this important and comprehensive work has been completely revised and a vast amount of new material has been incorporated in the text.

Dr. Case is to be congratulated on his excellent translation of the German text; he has supplied a much-needed augmented bibliography.

The numerous illustrations, some 1300 in all, are clear and well produced. We are confident that this English edition will be sold out as quickly as former ones.

This work should interest not only the radiologists, orthopædic surgeons, and pathologists, but also members of the legal profession who wish to find out for themselves information concerning the borderlines of the normal and early pathological variants of the bones of the skeleton.

Cardiac Pressures and Pulses. A Manual of Right and Left Heart Catheterization. By ALDO A. LUISADA, M.D., Chicago Medical School; and CHI KONG LIU, M.D., Chicago Medical School. 10 × 6¾ in. Pp. 116 + viii, with 51 illustrations. 1956. New York and London: Grune & Stratton. $6.00.

THIS rather slender volume is described as a manual of right and left heart catheterization and should be of value to all who have to deal with cardiac cases, whether medical or surgical. It should be useful to the beginner in cardiac catheterization, but it is doubtful if it will help those of more than moderate experience.

The tiresome habit of numbering the references instead of using the Harvard system tells against smooth reading, as also does the liberal use of that outmoded nuisance, the footnote.

The arrangement of text and pressure tracings is very unsatisfactory. The letterpress repeatedly ends as if the chapter has been completed, but on turning the page this is found not to be so. This surely can and should be corrected.

It is a pity that the important subject of differentiation between mitral stenosis and mitral regurgitation by pressure tracings from the left atrium is presented sketchily and unconvincingly and is supported only by 'scheme' tracings and not genuine ones.

The monograph contains much helpful material, although the cost is about twice what it should be.

Bases physiologiques de la Chirurgie neuro-vasculaire. By CH. MENTHA, Privat-docent à la Faculté de Genève. With a Foreword by Professor RENÉ LERICHE. 9¾ × 6½ in. Pp. 149 + viii, with 32 illustrations. 1956. Paris: Masson. 1000 fr.

THIS is a review of our present knowledge of the sympathetic nervous system with its clinical applications and the effects of various forms of interference with it. The book is dedicated to, and introduced by, the late Professor René Leriche, who draws attention to the wide experience of the author, who has worked in Boston as well as in France. Both of them have always had doubts of the existence of vasodilator fibres in the sympathetic system. Leriche regards one of the most important contributions, the concept of "l'assistance mutuelle des territoires vasculaires", a constant association of vasodilation and vasoconstriction in adjacent territories. A chapter on the history of our knowledge of the sympathetic is followed by others on the cerebral control of vasomotor reactions, the central and peripheral pathways and the effects of

preganglionectomy, ganglionectomy, and peripheral nerve sections. Consideration is given to the sympathetic innervation of the limbs and of particular structures such as the iris. Some thirty figures, mostly line drawings, diagrams, and charts, illustrate the text and there is a fairly complete bibliography. A good deal of the text of this book is speculative but it is a thoughtful presentation which no one who is seriously interested in the sympathetic system can afford to overlook.

Surgery of the Hand. By STERLING BUNNELL, M.D. Third edition. 10¼ × 7¼ in. Pp. 1079 + xvi, with 1047 illustrations and 9 coloured plates. 1956. London: Pitman Medical Publishing Co. Ltd. £7 7s.

IN this modern traumatic age the surgery of the hand is of the utmost importance to every surgeon both at home and abroad. With the introduction of antibiotics hand surgery has advanced to a vast extent. Dr. Bunnell has an international reputation as a surgeon who has for many years devoted his energies to the surgery of the hand. His new edition remains a classic in surgical literature and the 200 new illustrations will enhance the value of this book. Among the recent advances which are covered in this edition are those dealing with the use and abuse of antibiotics, cross-finger flaps, exercise after tendon repair, contraction and paralysis of the intrinsic muscles, reconstruction of the thumb, burns, and seal finger.

An important reference book.

Urology. Edited by MEREDITH CAMPBELL, M.S., M.D., F.A.C.S., New York. With the collaboration of 51 contributors. In three volumes. 9¾ × 6¾ in. Pp. 2356 + complete index in each volume. 1148 illustrations. 1954. Philadelphia and London: W. B. Saunders Co. £15.

THIS is the most comprehensive and detailed work on urology that has yet been written.

Professor Campbell has indeed been fortunate in his fifty-one contributors, each of whom writes on his own particular subject.

Since the second world war urology has become a speciality of its own and great strides have been made in this branch of medicine and surgery.

These three large volumes are beautifully illustrated with some 1148 figures, all of which have been well chosen. Some illustrations are outstanding, such as those on renal angiography and many of the pylograms and photomicrographs.

A very complete survey is given of the tumours of the urogenital system and this in itself is most useful from the point of view of reference.

An excellent account of the neurophysiology of micturition is presented in the second volume. The vast subject of urology in infancy and childhood is well covered and much recent research work in this field has been incorporated. The surgery of the ureter and the various modern operative procedures carried out upon it are well described and illustrated.

The work includes an interesting and important section dealing with medical diseases of the kidney; this should interest all surgeons who practise urology.

These volumes will remain the reference work on urology for many years to come.

Cancer of the Esophagus and the Stomach. By OWEN H. WANGENSTEEN, M.D., Minneapolis. Second edition. 9⅜ × 6¼ in. Pp. 144, with 60 illustrations. 1956. New York: American Cancer Society.

THE second edition of this small monograph has been carefully revised and contains up-to-date vital statistics dealing with cancer of the stomach. An interesting chapter on cancer detection and the work in cancer centres shows that several early cases have been detected and, therefore, more centres are advocated.

The Year Book of Orthopedics and Traumatic Surgery, 1955-1956. Edited by EDWARD L. COMPERE, M.D., F.A.C.S., F.I.C.S., Professor and Chairman, Department of Orthopedic Surgery, Northwestern University Medical School; etc. 7½ × 5⅛ in. Pp. 333, with 211 illustrations. 1955. Chicago: Year Book Publishers Inc. (London: Interscience Publishers Ltd.) 49s.

THIS year-book of orthopædics gives an excellent epitome of all the progress in this subject which has been reported in the literature during the last year.

Injuries of the spine and bones have received due emphasis.

It is interesting to note that the Salk vaccine for poliomyelitis has been declared to be about 80 per cent effective, and that very shortly there will be an adequate supply of vaccine, which has been proved to be safe for use, to vaccinate all the children of the United States.

Traumatic injuries and their treatment seem to become more numerous as the years go by.

It is interesting to read that Syme's amputation is coming into its own again and is considered better than a below-knee amputation. Failures of the Syme's amputation are the result of poor selection of cases or faulty surgical technique.

This Year Book will prove of real value to those surgeons who wish to keep abreast of modern progress.

The Year Book of Neurology, Psychiatry, and Neurosurgery, 1955-1956. Edited by ROLAND P. MACKAY, M.D. (Neurology); S. BERNARD WORTIS, M.D. (Psychiatry); PERCIVAL BAILEY, M.D., and OSCAR SUGAR, M.D. (Neurosurgery). 7⅝ × 5⅛ in. Pp. 576, with 97 illustrations. 1956. Chicago: Year Book Publishers Inc. (London: Interscience Publishers Ltd.) 53s.

THE many contributions to neurology and its allied subjects covered by this annual review are recorded in succinct but easily readable form, enhanced in value by editorial comments which are often terse but very much to the point.

The outstanding neurological event of 1955 is regarded as the development of a protective vaccine against acute anterior poliomyelitis—and the evidence for its efficacy is discussed. During the year, also, there have been developments in our knowledge of the functions of the temporal lobes, the inferior and medial portions of which are apparently indispensable to memory. Temporal lobectomy for psychomotor epilepsy was introduced in 1951 by Bailey and Gibbs, who warned surgeons against invading the medial part of both lobes; but, despite this, the bilateral operation has been done, with appalling results on the personality of the patient, who subsequently failed to recognize even closest relatives and had other complications. The case reported should emphasize this warning.

It is interesting to note the increasing strength of the reaction against leucotomy or lobotomy for mental diseases, and that since 1950 the operation has been forbidden in Soviet Russia. It is strongly condemned as a means of reducing aggressive tendencies and agitation in patients in mental hospitals and has been described in these cases as "a form of administrative lethargy". ("Such patients are still less trouble if one puts them in a gas-chamber as the Nazis did.") It is being much less often performed in mental hospitals to-day and the comment is made that perhaps its only justification is the relief of violent suffering when it is often enough to

operate on only one frontal lobe and thereby with less impairment of personality. As the distinguished editors of the section on neurosurgery remark, it all boils down to the Hippocratic maxim, " primum non nocere ".

The book provides a ready means of keeping up to date for all who are interested in the recent contributions to the extensive field of neurology and its associated subjects, which it covers in its 550-odd pages of careful condensation.

Diseases of the Heart and Circulation. By PAUL WOOD, O.B.E., M.D. (Melbourne), F.R.C.P. (Lond.), Director, Institute of Cardiology, London ; Physician, National Heart Hospital ; Physician in Charge, Cardiac Department, Brompton Hospital. Second edition. 9½ × 6½ in. Pp. 1005 + xl, with many illustrations. 1956. London : Eyre & Spottiswoode. £5 5s.

SOME years ago it would have been considered curious, to say the least, to review a book on diseases of the heart in a surgical journal. But to-day direct cardiac surgery is practised all over the world. Mitral valvotomy and aortic valvotomy are giving good results. This being so, it behoves all surgeons who practise cardiac surgery to have an intimate knowledge of the diseases of the heart.

This new and enlarged edition opens with two virtually new chapters on symptoms and signs, the modern interpretation of which has been clearly and fully described in the light of recent discoveries.

The whole modern findings on mitral, aortic, and tricuspid valve disease, particularly in relation to cardiac surgery, have been brought into this book. Fresh material has been added on modern treatment by antibiotics.

The medical treatment of hypertension, notably in respect of hexamethonium, ansolysen, reserpine, and other hypotensive agents, is discussed at length. The book is well illustrated and the electrocardiograms are excellently produced.

This second edition is in our opinion bound to be as popular as its predecessor, as it is a most readable and important work.

Psychosomatic Aspects of Surgery. Edited by ALFRED J. CANTOR, M.D., and ARTHUR N. FOXE, M.D. The Proceedings of the First Annual Meeting of the Academy of Psychosomatic Medicine, held in New York City, October, 1954. 8½ × 5½ in. Pp. 220 + xii. 1956. New York and London : Grune & Stratton Inc. $6.50.

THIS is an account in book form of the proceedings of the first annual meeting of the Academy of Psychosomatic Medicine, which was held in New York City in October, 1954. Hans Selye, of Montreal, writes a foreword in which he points out that although ' psychosomatic ' is a comparatively new term, few if any other medical topics have engendered as many spoken or written words as the problems relating to the interactions between mind and body. The sexualization of organs will perhaps be a little deep for most surgeons, but such topics as " what patients should be told, especially about malignant disease ", and " postconcussional headache and psychosomatic symptoms " are of interest. We are given sound advice such as, " Let us have a care lest our own psychologic needs dictate what we say rather than the needs of the patient " and " the surgeon who constantly shows that he is tense and anxious is a serious psychosomatically noxious agent for most patients ". This might have been stated a little more simply and some of the expressions are a little unusual to English readers, such as the " patient's mentation " and " psychotherapy ' at the grass roots ' ", but throughout the chapters and discussions on various branches of surgery, including anæsthesia and gynæcology, there is much which will be provocative of thought in the surgical reader.

Proctology. By HARRY E. BACON, B.S., M.D., Sc.D., LL.D., F.A.C.S., STUART T. ROSS, A.B., M.D., F.A.C.S., and PORFIRIO MAYO RECIO, B.S., M.D., M.Sc. 9 × 6 in. Pp. 441 + xiv, with 228 illustrations and 5 coloured plates. 1956. Philadelphia : J. B. Lippincott Co. (London : Pitman Medical Publishing Co. Ltd.) 80s.

THIS is a profusely illustrated book dealing with rectal diseases and some lesions of the sigmoid colon. It is just a reference book for the practitioner and contains little that can be of value to the general surgeon. Some of the illustrations are too diagrammatic and give the reader a distorted idea of the condition under consideration.

There is surely no need to illustrate four different articles which had been removed from the rectum. This book is not up to the standard of the British works on this subject.

Anatomy for Surgeons. By W. HENRY HOLLINSHEAD, Ph.D., Professor of Anatomy, Mayo Foundation, University of Minnesota. Volume 2 : The Thorax, Abdomen, and Pelvis. 10¼ × 7 in. Pp. 934 + xvi, with 678 illustrations. 1956. London : Cassell & Co. Ltd. £7 7s.

THIS large and important volume of nearly one thousand pages is profusely illustrated with excellent diagrammatic drawings. These drawings are just what the modern surgeon requires in his day-to-day work.

Professor Hollinshead has had the co-operation of the many heads of the various departments in the Mayo Clinic and, therefore, his book has a true clinical anatomical flavour.

This work on anatomy for surgeons will largely replace the books on applied anatomy because it is more comprehensive and more practical.

Surgeons the world over will find this work an important reference volume not only when looking up structural variations but also when contemplating some new operative exposure, and when considering a research programme.

Now our interests have been stimulated by the appearance of Volume 2 we look forward to reading Volume 3. Professor Hollinshead has put surgeons in his debt by producing an excellent volume.

The Invisible Flag. A Report by PETER BAMM, translated from the German by FRANK HERRMANN. 8½ × 5⅜ in. Pp. 229. 1956. London : Faber & Faber Ltd. 18s.

WE have many books dealing with the medical and surgical work of the second world war from the British and American standpoint ; but we know little concerning the conflict between the giant armies of Russia and Germany during the campaigns of 1941–5. This book, written by a surgeon in the German Army Medical Service, fills in a distinct gap in medical history.

It is difficult to imagine a horse-drawn front-line operating theatre, yet this is the place where Peter Bamm did most of his surgery. He operated upon soldiers of both sides and his patients ranged from privates to generals. He had many encounters with diverse actions and races of the Russian population, both civilian and military.

The author tells his story in a very interesting way and has the knack of making his facts stand out in the reader's mind.

An interesting book which should make an appeal to all surgeons everywhere.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

Anatomical Techniques. By D. H. TOMPSETT, B.Sc., Ph.D., Prosector to the Royal College of Surgeons of England. With a Foreword by SIR CECIL WAKELEY, Bart., K.B.E., C.B., LL.D., F.R.C.S. 10 × 6½ in. Pp. 240 + xvi, with 83 illustrations, 9 of which are in colour. 1956. Edinburgh: E. & S. Livingstone Ltd. 35s.

Lymphatics, Lymph and Lymphoid Tissue. By JOSEPH MENDIL YOFFEY, D.Sc., M.D. (Manch.), F.R.C.S. (Eng.), Professor of Anatomy, University of Bristol; and FREDERICK COLIN COURTICE, M.A., D.Phil. (Oxon.), D.Sc. (Sydney), F.R.A.C.S. (Hon.). 9½ × 6 in. Pp. 510 + viii, with 99 illustrations. 1956. London: Edward Arnold (Publishers) Ltd. 60s.

Orthopædic Nursing. By MARY POWELL, S.N.R., M.C.S.P., Orthopædic Nursing Certificate, Matron, Nuffield Orthopædic Centre, Oxford. With a Foreword by SIR REGINALD WATSON-JONES, B.Sc., M.Ch.Orth., F.R.C.S., F.R.C.S.Edin.(Hon.), F.R.A.C.S. (Hon.), F.A.C.S. (Hon.). Second edition. 8¾ × 5½ in. Pp. 440 + xii, with 271 illustrations. 1956. Edinburgh: E. & S. Livingstone Ltd. 27s. 6d.

Operative Surgery. Edited by CHARLES ROB, M.C., M.Chir., F.R.C.S., Professor of Surgery, St. Mary's Hospital, London; and RODNEY SMITH, M.S., F.R.C.S., Surgeon, St. George's Hospital, London. 11¼ × 8¾ in. Vol. 1, pp. 1–342 + xviii, with numerous illustrations. Vol. 2, pp. 343–547 + xii, with numerous illustrations. 1956. London: Butterworth & Co. (Publishers) Ltd. £5 10s. per volume.

A Manual of Human Anatomy. Volumes I, II, and III. By J. T. AITKEN, M.D., Reader in Anatomy at University College, London; G. CAUSEY, M.B., F.R.C.S., Professor of Anatomy, Royal College of Surgeons, London; J. JOSEPH, M.D., M.R.C.O.G., Reader in Anatomy, Guy's Hospital, London; and J. Z. YOUNG, M.A., F.R.S., Professor of Anatomy at University College, London. 8½ × 5½ in. *Volume I.* Thorax and Upper Limb, pp. 162 + viii, with 36 illustrations. *Volume II.* Head and Neck, pp. 180 + viii, with 53 illustrations. *Volume III.* Lower Limb, pp. 117 + viii, with 36 illustrations. 1956. Edinburgh: E. & S. Livingstone Ltd. Vol. I, 14s.; Vol. II, 16s.; Vol. III, 12s. 6d.

The Treatment of Fractures. By LORENZ BÖHLER, M.D., Director of the Accident Hospital, Vienna; Professor of Accident Surgery, University of Vienna. Volume I. Translated from the Thirteen German Editions by HANS TRETTER, HELEN B. LUCHINI, FRANK KRUEZ, OTTO A. RUSSE, and ROBERT G. B. BJOLNSON. 9¾ × 6¾ in. Pp. 1104 + xx, with 1721 illustrations. 1956. New York: Grune & Stratton. $24.50.

The Nuffield Foundation. Report for the Year ended March 21, 1956. 8½ × 5½ in. Pp. 160. 1956. London: The Nuffield Foundation.